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(71) Applicant (for all designated States except US): **ORIGENE TECHNOLOGIES, INC** [US/US]; 6 Taft Court, Suite 100, Rockville, MD 20850 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SUN, Zairen** [CN/US]; 1083 Copperstone Court, Rockville, MD 20852 (US). **JAY, Gilbert** [US/US]; 5801 Nicholson Lane, North Bethesda, MD 20852 (US).

(74) Agent: **LEBOVITZ, Richard, M.**; Origene Technologies, Inc., 6 Taft Court, Suite 100, Rockville, MD 20850 (US).

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(54) Title: **PROSTATE CANCER EXPRESSION PROFILES**

(57) Abstract: The present invention relates to all facets of novel polynucleotides, the polypeptides they encode, antibodies and specific binding partners thereto, and their applications to research, diagnosis, drug discovery, therapy, clinical medicine, forensic science and medicine, etc. The polynucleotides are differentially-regulated in prostate cancer and are therefore useful in variety of ways, including, but not limited to, as molecular markers, as drug targets, and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determining predisposition to, etc., diseases and conditions, to prostate cancer.

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## PROSTATE CANCER EXPRESSION PROFILES

This application claims the benefit U.S. Provisional Application No. 60/281,731, filed April 6, 2001, and U.S. Provisional Application No. 60/281,732, filed April 6, 2001, which are hereby incorporated by reference in their entirety.

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## DESCRIPTION OF THE DRAWINGS

Tables 1 and 2 list genes differentially-regulated in prostate cancer. "DNA SEQ ID" and "Prt SEQ ID" refer to the corresponding DNA and protein sequences in the attached sequence listing. The genes can alternatively be referred to by GenBank accession number in the fifth column ("GI#") or the "identifier" in the third column. The genes listed in Table 1 are up-regulated, and those in Table 2 are down-regulated ("Exp" refers to the expression profile, U is up-regulated expression, and D is down-regulated expression). The characterization of the gene under the "description" heading is based on its listing in GenBank. 5', 3', genomic sequences, etc., which correspond to the genes can be retrieved routinely from Genbank, e.g., by searching the accession number. SEQ ID NOS 1-107 are DNA, and 108-211 are polypeptide. These sequences, and all information referenced to the accession number, are incorporated by reference in their entirety.

The polypeptide sequences was analyzed for the presence of functional domains using the publicly available Pfam program. This information is summarized in Table 3. Domains present in each polypeptide are listed under "domain." Any abbreviations are those used in Pfam. The start of the domain is indicated by "seq-f" and the end of the domain by "seq-t." The "score" is the statistical score of this match to the domain in bits. In general, a higher score indicates a better match. "E" is the statistical score of this match in Evalve (frequentist) approach. The smaller score in this case shows a better match between the domain and the query sequence. For more information on the program and scoring, see, e.g., Sonnhammer et al., *Proteins: Structure, Function and Genetics* 28:405-420 (1997); Sonnhammer et al., *Nucleic Acids Research*, 26:320-322 (1998); Bateman et al., *Nucleic Acids Research*, 27:260-262 (1999); Bateman et al., *Nucleic Acids Research*, 28:263-266 (2000).

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## DESCRIPTION OF THE INVENTION

The present invention relates to all facets of novel polynucleotides, the polypeptides they encode, antibodies and specific binding partners thereto, and their applications to research, diagnosis, drug discovery, therapy, clinical medicine, forensic science and medicine, etc. The polynucleotides are differentially regulated in prostate cancer and are therefore useful in variety of ways, including, but not limited to, as molecular markers, as drug targets, and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determining predisposition to, etc., diseases and conditions,, especially relating to prostate cancer. The identification of specific genes, and groups of genes, expressed in pathways physiologically relevant to prostate cancer permits the definition of functional and disease pathways, and the delineation of targets in these pathways which are useful in diagnostic, therapeutic, and clinical applications. The present invention also relates to methods of using the polynucleotides and related products (proteins, antibodies, etc.) in business and computer-related methods, e.g., advertising, displaying, offering, selling, etc., such products for sale, commercial use, licensing, etc.

Prostate cancer is the most common form of cancer diagnosed in the American male, occurring predominantly in males over age 50. The number of men diagnosed with prostate cancer has steadily increased as a result of the increasing population of older men. The American Cancer Society estimates that in the year 2000, about 180,000 American men were diagnosed with prostate cancer and about 32,000 died from the disease. In comparison, 1998 estimates for lung cancer in men were 171,500 cases and 160,100 deaths, and for colorectal cancer, the estimates were 131,600 cases and 56,000 deaths. Despite these high numbers, 89 percent of men diagnosed with the disease will survive at least five years and 63 percent will survive at least 10 years.

Patients having prostate cancer display a wide range of phenotypes. In some men, following detection, the tumor remains a latent histological tumor and does not become clinically significant. However, in other men, the tumor progresses rapidly, metastasizing and killing the patient in a relatively short time. Prostate cancer can be cured if the tumor is confined to a small region of the gland and is discovered at early stage. In such cases, radiation or surgical removal often results in complete elimination of the disease. Frequently, however, the prostate cancer has already spread to surrounding tissue and metastasized to

remote locations. In these cases, radiation and other therapies, are less likely to effect a complete cure.

Androgen deprivation is a conventional therapy to treat prostate cancer. Androgen blockade can be achieved through several different routes. Androgen suppressive drugs include, e.g., Lupron (leuprolide acetate), Casodex (bicalutamide), Eulexin (flutamide), Nilandron (nilutamide), Zoladex (goserelin acetate implant), and Viadur (leuprolide acetate), which act through several different mechanisms. While these drugs may offer remission and tumor regression in many cases, often the therapeutic effects are only temporary. Prostate tumors lose their sensitivity to such treatments, and become androgen-independent. Thus, new therapies are clearly needed.

The first clinical symptoms of prostate cancer are typically urinary disturbances, including painful and more frequent urination. Diagnosis for prostate cancer is usually accomplished using a combination of different procedures. Since the prostate is located next to the rectum, rectal digital examination allows the prostate to be examined manually for the presence of hyperplasia and abnormal tissue masses. Usually, this is the first line of detection. If a palpable mass is observed, a blood specimen can be assayed for prostate-specific antigen (PSA). Very little PSA is present in the blood of a healthy individual, but BPH and prostate cancer can cause large amounts of PSA to be released into the blood, indicating the presence of diseased tissue. Definitive diagnosis is generally accomplished by biopsy of the prostate tissue.

No single gene or protein has been identified which is responsible for the etiology of all prostate cancers. Although PSA is widely used as a diagnostic reagent, it has limitations in its sensitivity and its ability to detect early cancers. It is estimated that approximately 20% to 30% of tumors will be missed when PSA is used alone. It is likely that diagnostic and prognostic markers for prostate cancer disease will involve the identification and use of many different genes and gene products to reflect its multifactorial origin.

A continuing goal is to characterize the gene expression patterns of the various prostate cancers to genetically differentiate them, providing important guidance in preventing and treating cancers. Molecular pictures of cancer, such as the pattern of differentially-regulated genes identified herein, provide an important tool for molecularly dissecting and classifying cancer, identifying drug targets, providing prognosis and therapeutic information, etc. For instance, an array of polynucleotides corresponding to genes differentially regulated in prostate cancer can be used to screen tissue samples for the existence of cancer, to



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categorize the cancer (e.g., by the particular pattern observed), to grade the cancer (e.g., by the number of differentially-regulated genes and their amounts of expression), to identify the source of a secondary tumor, to screen for metastatic cells, etc. These arrays can be used in combination with other markers, e.g., PSA, PMSA (prostate membrane specific antigen), or  
5 any of the grading systems used in clinical medicine.

As indicated by these studies, cancer is a highly diverse disease. Although all cancers share certain characteristics, the underlying cause and disease progression can differ significantly from patient to patient. So far, over a dozen distinct genes have been identified which, when mutant, result in a cancer. In breast cancer, alone, a handful of different genes  
10 have been isolated which either cause the cancer, or produce a predisposition to it. As a consequence, disease phenotypes for a particular cancer do not look all the same. In addition to the differences in the gene(s) responsible for the cancer, heterogeneity among individuals, e.g., in age, health, sex, and genetic background, can also influence the disease and its progression. Gene penetrance, in particular, can vary widely among population members.  
15 Recent studies have shown tremendous diversity in gene expression patterns among cancer patients. For these and other reasons, one gene/polypeptide target alone can be insufficient to diagnose or treat a cancer. Even a gene which is highly differentially-expressed and penetrant in cancer patients may not be so highly expressed in all patients and at all stages of the cancer. By selecting a set of genes and/or the polypeptides they encode, cancer  
20 diagnostics and therapeutics can be designed which effectively diagnose and treat a population of diseased individuals, rather than only a small handful when single genes are targeted.

#### Nucleic acids

25 In accordance with the present invention, genes have been identified which are differentially expressed in prostate cancer. Tables 1 and 2 list of genes which are differentially-regulated in the cancer. These genes can be further divided into groups based on additional characteristics of their expression and the tissues in which they are expressed. For instance, genes can be further subdivided based on the stage and/or grade of the cancer in  
30 which they are expressed. Genes can also be grouped based on their penetrance in a prostate cancer, e.g., expressed in all prostate cancer examined, expressed in a certain percentage of prostate cancer examined, etc. Additionally, genes can be categorized by their function and/or the polypeptides they encode. This includes, but is not limited to, cellular

localization, functional activity (e.g., kinase, cytoskeletal element, or transcriptional factor), functional pathway (e.g., protein manufacture, cell signaling, cell movement, cell adhesion, responsivity to cAMP, energy production, etc.), etc. These groupings do not restrict or limit the use such genes in therapeutic, diagnostic, prognostic, etc., applications. For instance, a  
5 gene which is expressed in only some cancers (e.g., incompletely penetrant) may be useful in therapeutic applications to treat a subset of cancers. Similarly, a co-penetrant gene, or a gene which is expressed in prostate cancer and other normal tissues, may be useful as a therapeutic or diagnostic, even if its expression pattern is not highly prostate specific. Thus, the uses of the genes or their products are not limited by their patterns of expression.

10 For genes which are differentially-regulated, gene and protein replacement therapies can be used therapeutically to restore expression levels to normal. When a protein product is to be administered, secreted proteins are more likely to be targets for replacement therapy than intracellular and membrane-bound proteins. For the latter classes, gene therapy may be a more effective means of delivery, e.g., administering a gene which is expressed inside a cell  
15 on or on its surface.

By the phrase "differential expression," it is meant that the levels of expression of a gene, as measured by its transcription or translation product, are different depending upon the specific cell-type or tissue (e.g., in an averaging assay that looks at a population of cells). There are no absolute amounts by which the gene expression levels must vary, as long as the  
20 differences are measurable.

The phrase "down-regulated" indicates that an mRNA transcript or other nucleic acid corresponding to a polynucleotide of the present invention is expressed in lower amounts in a cancer as compared to the same transcript expressed in normal cells from which the cancer was derived. In general, down-regulation can be assessed by any suitable method, including  
25 any of the nucleic acid detection and hybridization methods mentioned below, as well as polypeptide-based methods. Down-regulation also includes going from substantially no expression in a normal tissue, from detectable expression in a normal tissue, from significant expression in a normal tissue, to higher levels in the cancer.

The phrase "up-regulated" indicates that an mRNA transcript or other nucleic acid  
30 corresponding to a polynucleotide of the present invention is expressed in larger amounts in a cancer as compared to the same transcript expressed in normal cells from which the cancer was derived. For instance, a gene's up-regulation can be determined by comparing its abundance per gram of RNA (e.g., total RNA, polyadenylated mRNA, etc.) extracted from a

cancer tissue in comparison to the corresponding normal tissue. The normal tissue can be from the same or different individual or source. For convenience, it can be supplied as a separate component or in a kit in combination with probes and other reagents for detecting genes. The quantity by which a nucleic acid is up-regulated can be any value, e.g., more than  
5 10%, 50%, 2-fold, 5-fold, 10-fold, etc. Up-regulation also includes going from substantially no expression, to detectable expression, to significant or highly restricted expression, etc.

Differential regulation can be determined by any suitable method, e.g., by comparing its abundance per gram of RNA (e.g., total RNA, polyadenylated mRNA, etc.) extracted from a prostate tissue in comparison to the corresponding normal tissue. The normal tissue can be  
10 from the same or different individual or source. For convenience, it can be supplied as a separate component or in a kit in combination with probes and other reagents for detecting genes. The quantity by which a nucleic acid is differentially-regulated can be any value, e.g., about 10% more or less of normal expression, about 50% more or less of normal expression, 2-fold more or less, 5-fold more or less, 10-fold more or less, etc.

15 The amount of transcript can also be compared to a different gene in the same sample, especially a gene whose abundance is known and substantially no different in its expression between normal and cancer cells (e.g., a "control" gene). If represented as a ratio, with the quantity of differentially-regulated gene transcript in the numerator and the control gene transcript in the denominator, the ratio would be larger, e.g., in breast cancer than in a sample  
20 from normal breast tissue.

Differential-regulation can arise through a number of different mechanisms. The present invention is not bound by any specific way through which it occurs. Differential-regulation of a polynucleotide can occur, e.g., by modulating (1) transcriptional rate of the gene (e.g., increasing its rate, inducing or stimulating its transcription from a basal, low-level  
25 rate, etc.), (2) the post-transcriptional processing of RNA transcripts, (3) the transport of RNA from the nucleus into the cytoplasm, (4) RNA nuclear and cytoplasmic turnover and polypeptide turnover (e.g., by virtue of having higher stability or resistance to degradation), and combinations thereof. See, e.g., Tollervey and Caceras, *Cell*, 103:703-709, 2000.

A differentially-regulated polynucleotide is useful in a variety of different  
30 applications as described in greater details below. Because it is more abundant in cancer, it and its expression products can be used in a diagnostic test to assay for the presence of cancer, e.g., in tissue sections, in a biopsy sample, in total RNA, in lymph, in blood, etc. Differentially-regulated polynucleotides and polypeptides can be used individually, or in

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groups, to assess the cancer, e.g., to determine the specific type of cancer, its stage of development, the nature of the genetic defect, etc., or to assess the efficacy of a treatment modality. How to use polynucleotides in diagnostic and prognostic assays is discussed below. In addition, the polynucleotides and the polypeptides they encode, can serve as a target for therapy or drug discovery. A polypeptide, coded for by a differentially-regulated polynucleotide, which is displayed on the cell-surface, can be a target for immunotherapy to destroy, inhibit, etc., the diseased tissue. Differentially-regulated transcripts can also be used in drug discovery schemes to identify pharmacological agents which suppress, inhibit, etc., their differential-regulation, thereby preventing the phenotype associated with their expression. Thus, a differentially-regulated polynucleotide and its expression products of the present invention have significant applications in diagnostic, therapeutic, prognostic, drug development, and related areas.

The expression patterns of the differentially expressed genes disclosed herein can be described as a "fingerprint" in that they are a distinctive pattern displayed by a cancer. Just as with a fingerprint, an expression pattern can be used as a unique identifier to characterize the status of a tissue sample. The list of genes represented in Tables 1 and 2 provide an example of a cell expression profile for a prostate cancer. It can be used as a point of reference to compare and characterize unknown samples and samples for which further information is sought. Tissue fingerprints can be used in many ways, e.g., to classify an unknown tissue as being a prostate cancer, to determine the origin of a particular cancer (e.g., the origin of metastatic cells), to determine the presence of a cancer in a biopsy sample, to assess the efficacy of a cancer therapy in a human patient or a non-human animal model, to detect circulating cancer cells in blood or a lymph node biopsy, etc. While the expression profile of the complete gene set represented in Tables 1 and 2 may be most informative, a fingerprint containing expression information from less than the full collection can be useful, as well. In the same way that an incomplete fingerprint may contain enough of the pattern of whorls, arches, loops, and ridges, to identify the individual, a cell expression fingerprint containing less than the full complement may be adequate to provide useful and unique identifying and other information about the sample. Moreover, cancer is a multifactorial disease, involving genetic aberrations in more than gene locus. This multifaceted nature may be reflected in different cell expression profiles associated with breast cancers arising in different individuals, in different locations in the same individual, or even within the same cancer locus. As a result, a complete match with a particular cell expression profile, as

shown herein, is not necessary to classify a cancer as being of the same type or stage.

Similarity to one cell expression profile, e.g., as compared to another, can be adequate to classify cancer types, grades, and stages. SEQ ID NOS 1-211 are referred to generally as "genes" to indicate that they represent specific gene loci, and are not limited to the particular nucleotide and polypeptide sequences disclosed herein. For example, fibronectin (SEQ ID NO 60 and 196) is up-regulated in prostate cancers. Probes to detect its up regulation can be selected from the attached specific sequences, as well as genomic, upstream, downstream, and intron sequences which are not in the attached sequence listing.

A mammalian polynucleotide, or fragment thereof, of the present invention is a polynucleotide having a nucleotide sequence obtainable from a natural source. It therefore includes naturally-occurring normal, naturally-occurring mutant, and naturally-occurring polymorphic alleles (e.g., SNPs), differentially-spliced transcripts, splice-variants, etc. By the term "naturally-occurring," it is meant that the polynucleotide is obtainable from a natural source, e.g., animal tissue and cells, body fluids, tissue culture cells, forensic samples. Natural sources include, e.g., living cells obtained from tissues and whole organisms, tumors, cultured cell lines, including primary and immortalized cell lines. Naturally-occurring mutations can include deletions (e.g., a truncated amino- or carboxy-terminus), substitutions, inversions, or additions of nucleotide sequence. These genes can be detected and isolated by polynucleotide hybridization according to methods which one skilled in the art would know, e.g., as discussed below.

A polynucleotide according to the present invention can be obtained from a variety of different sources. It can be obtained from DNA or RNA, such as polyadenylated mRNA or total RNA, e.g., isolated from tissues, cells, or whole organism. The polynucleotide can be obtained directly from DNA or RNA, from a cDNA library, from a genomic library, etc. The polynucleotide can be obtained from a cell or tissue (e.g., from an embryonic or adult tissues) at a particular stage of development, having a desired genotype, phenotype, disease status, etc.

The genes described in Tables 1 and 2 can be partial sequences that correspond to full-length, naturally-occurring transcripts. The present invention includes, as well, full-length polynucleotides that comprise these partial sequences, e.g., genomic DNAs and polynucleotides comprising a start and stop codon, a start codon and a polyA tail, a transcription start and a polyA tail, etc. These sequences can be obtained by any suitable method, e.g., using a partial sequence as a probe to select a full-length cDNA from a library

containing full-length inserts. A polynucleotide which "codes without interruption" refers to a polynucleotide having a continuous open reading frame ("ORF") as compared to an ORF which is interrupted by introns or other noncoding sequences.

## 5 Genomic

The present invention also relates genomic DNA from which the polynucleotides of the present invention can be derived. A genomic DNA coding for a human, mouse, or other mammalian polynucleotide, can be obtained routinely, for example, by screening a genomic library (e.g., a YAC library) with a polynucleotide of the present invention, or by searching  
10 nucleotide databases, such as GenBank and EMBL, for matches. Promoter and other regulatory regions can be identified upstream of coding and expressed RNAs, and assayed routinely for activity, e.g., by joining to a reporter gene (e.g., CAT, GFP, alkaline phosphatase, luciferase, galactosidase). A promoter obtained from a prostate selective gene can be used, e.g., in gene therapy to obtain tissue-specific expression of a heterologous gene  
15 (e.g., coding for a therapeutic product or cytotoxin).

## Constructs

A polynucleotide of the present invention can comprise additional polynucleotide sequences, e.g., sequences to enhance expression, detection, uptake, cataloging, tagging, etc.  
20 A polynucleotide can include only coding sequence; a coding sequence and additional non-naturally occurring or heterologous coding sequence (e.g., sequences coding for leader, signal, secretory, targeting, enzymatic, fluorescent, antibiotic resistance, and other functional or diagnostic peptides); coding sequences and non-coding sequences, e.g., untranslated sequences at either a 5' or 3' end, or dispersed in the coding sequence, e.g., introns.  
25 A polynucleotide according to the present invention also can comprise an expression control sequence operably linked to a polynucleotide as described above. The phrase "expression control sequence" means a polynucleotide sequence that regulates expression of a polypeptide coded for by a polynucleotide to which it is functionally ("operably") linked. Expression can be regulated at the level of the mRNA or polypeptide. Thus, the expression  
30 control sequence includes mRNA-related elements and protein-related elements. Such elements include promoters, enhancers (viral or cellular), ribosome binding sequences, transcriptional terminators, etc. An expression control sequence is operably linked to a nucleotide coding sequence when the expression control sequence is positioned in such a

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manner to effect or achieve expression of the coding sequence. For example, when a promoter is operably linked 5' to a coding sequence, expression of the coding sequence is driven by the promoter. Expression control sequences can include an initiation codon and additional nucleotides to place a partial nucleotide sequence of the present invention in-frame in order to produce a polypeptide (e.g., pET vectors from Promega have been designed to permit a molecule to be inserted into all three reading frames to identify the one that results in polypeptide expression). Expression control sequences can be heterologous or endogenous to the normal gene.

A polynucleotide of the present invention can also comprise nucleic acid vector sequences, e.g., for cloning, expression, amplification, selection, etc. Any effective vector can be used. A vector is, e.g., a polynucleotide molecule which can replicate autonomously in a host cell, e.g., containing an origin of replication. Vectors can be useful to perform manipulations, to propagate, and/or obtain large quantities of the recombinant molecule in a desired host. A skilled worker can select a vector depending on the purpose desired, e.g., to propagate the recombinant molecule in bacteria, yeast, insect, or mammalian cells. The following vectors are provided by way of example. Bacterial: pQE70, pQE60, pQE-9 (Qiagen), pBS, pD10, Phagescript, phiX174, pBK Phagemid, pNH8A, pNH16a, pNH18Z, pNH46A (Stratagene); Bluescript KS+II (Stratagene); ptrc99a, pKK223-3, pKK233-3, pDR54 0, pRIT5 (Pharmacia). Eukaryotic: PWLNEO, pSV2CAT, pOG44, pXT1, pSG (Stratagene), pSVK3, PBPV, PMSG, pSVL (Pharmacia), pCR2.1/TOPO, pCRII/TOPO, pCR4/TOPO, pTrcHisB, pCMV6-XL4, etc. However, any other vector, e.g., plasmids, viruses, or parts thereof, may be used as long as they are replicable and viable in the desired host. The vector can also comprise sequences which enable it to replicate in the host whose genome is to be modified.

## Hybridization

Polynucleotide hybridization, as discussed in more detail below, is useful in a variety of applications, including, in gene detection methods, for identifying mutations, for making mutations, to identify homologs in the same and different species, to identify related members of the same gene family, in diagnostic and prognostic assays, in therapeutic applications (e.g., where an antisense polynucleotide is used to inhibit expression), etc.

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The ability of two single-stranded polynucleotide preparations to hybridize together is a measure of their nucleotide sequence complementarity, e.g., base-pairing between nucleotides, such as A-T, G-C, etc. The invention thus also relates to polynucleotides, and their complements, which hybridize to a polynucleotide comprising a nucleotide sequence as set forth in Tables 1 and 2 and genomic sequences thereof. A nucleotide sequence hybridizing to the latter sequence will have a complementary polynucleotide strand, or act as a template for one in the presence of a polymerase (i.e., an appropriate polynucleotide synthesizing enzyme). The present invention includes both strands of polynucleotide, e.g., a sense strand and an anti-sense strand.

Hybridization conditions can be chosen to select polynucleotides which have a desired amount of nucleotide complementarity with the nucleotide sequences set forth in Tables 1 and 2 and genomic sequences thereof. A polynucleotide capable of hybridizing to such sequence, preferably, possesses, e.g., about 70%, 75%, 80%, 85%, 87%, 90%, 92%, 95%, 97%, 99%, or 100% complementarity, between the sequences. The present invention particularly relates to polynucleotide sequences which hybridize to the nucleotide sequences set forth in Tables 1 and 2 or genomic sequences thereof, under low or high stringency conditions. These conditions can be used, e.g., to select corresponding homologs in non-human species.

Polynucleotides which hybridize to polynucleotides of the present invention can be selected in various ways. Filter-type blots (i.e., matrices containing polynucleotide, such as nitrocellulose), glass chips, and other matrices and substrates comprising polynucleotides (short or long) of interest, can be incubated in a prehybridization solution (e.g., 6X SSC, 0.5% SDS, 100 µg/ml denatured salmon sperm DNA, 5X Denhardt's solution, and 50% formamide), at 22-68°C, overnight, and then hybridized with a detectable polynucleotide probe under conditions appropriate to achieve the desired stringency. In general, when high homology or sequence identity is desired, a high temperature can be used (e.g., 65 °C). As the homology drops, lower washing temperatures are used. For salt concentrations, the lower the salt concentration, the higher the stringency. The length of the probe is another consideration. Very short probes (e.g., less than 100 base pairs) are washed at lower temperatures, even if the homology is high. With short probes, formamide can be omitted. See, e.g., *Current Protocols in Molecular Biology*, Chapter 6, Screening of Recombinant Libraries; Sambrook et al., *Molecular Cloning*, 1989, Chapter 9.



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For instance, high stringency conditions can be achieved by incubating the blot overnight (e.g., at least 12 hours) with a long polynucleotide probe in a hybridization solution containing, e.g., about 5X SSC, 0.5% SDS, 100 µg/ml denatured salmon sperm DNA and 50% formamide, at 42°C. Blots can be washed at high stringency conditions that allow, e.g.,  
5 for less than 5% bp mismatch (e.g., wash twice in 0.1% SSC and 0.1% SDS for 30 min at 65°C), i.e., selecting sequences having 95% or greater sequence identity.

Other non-limiting examples of high stringency conditions includes a final wash at 65°C in aqueous buffer containing 30 mM NaCl and 0.5% SDS. Another example of high stringent conditions is hybridization in 7% SDS, 0.5 M NaPO<sub>4</sub>, pH 7, 1 mM EDTA at 50°C,  
10 e.g., overnight, followed by one or more washes with a 1% SDS solution at 42°C.

Whereas high stringency washes can allow for less than 5% mismatch, reduced or low stringency conditions can permit up to 20% nucleotide mismatch. Hybridization at low stringency can be accomplished as above, but using lower formamide conditions, lower temperatures and/or lower salt concentrations, as well as longer periods of incubation time.

15 Hybridization can also be based on a calculation of melting temperature (T<sub>m</sub>) of the hybrid formed between the probe and its target, as described in Sambrook et al..

Generally, the temperature T<sub>m</sub> at which a short oligonucleotide (containing 18 nucleotides or fewer) will melt from its target sequence is given by the following equation: T<sub>m</sub> = (number of A's and T's) x 2°C + (number of C's and G's) x 4°C. For longer molecules,  
20 T<sub>m</sub> = 81.5 + 16.6 log<sub>10</sub>[Na<sup>+</sup>] + 0.41(%GC) - 600/N where [Na<sup>+</sup>] is the molar concentration of sodium ions, %GC is the percentage of GC base pairs in the probe, and N is the length. Hybridization can be carried out at several degrees below this temperature to ensure that the probe and target can hybridize. Mismatches can be allowed for by lowering the temperature even further.

25 Stringent conditions can be selected to isolate sequences, and their complements, which have, e.g., at least about 90%, 95%, or 97%, nucleotide complementarity between the probe (e.g., a short polynucleotide of Tables 1 and 2 or genomic sequences thereof) and a target polynucleotide.

Other homologs of polynucleotides of the present invention can be obtained from  
30 mammalian and non-mammalian sources according to various methods. For example, hybridization with a polynucleotide can be employed to select homologs, e.g., as described in Sambrook et al., *Molecular Cloning*, Chapter 11, 1989. Such homologs can have varying amounts of nucleotide and amino acid sequence identity and similarity to such

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polynucleotides of the present invention. Mammalian organisms include, e.g., mice, rats, monkeys, pigs, cows, etc. Non-mammalian organisms include, e.g., vertebrates, invertebrates, zebra fish, chicken, *Drosophila*, *C. elegans*, *Xenopus*, yeast such as *S. pombe*, *S. cerevisiae*, roundworms, prokaryotes, plants, *Arabidopsis*, *artemia*, viruses, etc. The  
5 degree of nucleotide sequence identity between human and mouse can be about, e.g. 70% or more, 85% or more for open reading frames, etc.

#### Alignment

Alignments can be accomplished by using any effective algorithm. For pairwise  
10 alignments of DNA sequences, the methods described by Wilbur-Lipman (e.g., Wilbur and Lipman, *Proc. Natl. Acad. Sci.*, 80:726-730, 1983) or Martinez/Needleman-Wunsch (e.g., Martinez, *Nucleic Acid Res.*, 11:4629-4634, 1983) can be used. For instance, if the Martinez/Needleman-Wunsch DNA alignment is applied, the minimum match can be set at 9, gap penalty at 1.10, and gap length penalty at 0.33. The results can be calculated as a  
15 similarity index, equal to the sum of the matching residues divided by the sum of all residues and gap characters, and then multiplied by 100 to express as a percent. Similarity index for related genes at the nucleotide level in accordance with the present invention can be greater than 70%, 80%, 85%, 90%, 95%, 99%, or more. Pairs of protein sequences can be aligned by the Lipman-Pearson method (e.g., Lipman and Pearson, *Science*, 227:1435-1441, 1985)  
20 with k-tuple set at 2, gap penalty set at 4, and gap length penalty set at 12. Results can be expressed as percent similarity index, where related genes at the amino acid level in accordance with the present invention can be greater than 65%, 70%, 75%, 80%, 85%, 90%, 95%, 99%, or more. Various commercial and free sources of alignment programs are available, e.g., MegAlign by DNA Star, BLAST (National Center for Biotechnology  
25 Information), BCM (Baylor College of Medicine) Launcher, etc.

Percent sequence identity can also be determined by other conventional methods, e.g., as described in Altschul et al., *Bull. Math. Bio.* 48: 603-616, 1986 and Henikoff and Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915-10919, 1992.

#### 30 Specific polynucleotide probes

A polynucleotide of the present invention can comprise any continuous nucleotide sequence of Tables 1 and 2, sequences which share sequence identity thereto, or complements thereof. The term "probe" refers to any substance that can be used to detect,

identify, isolate, etc., another substance. A polynucleotide probe is comprised of nucleic acid can be used to detect, identify, etc., other nucleic acids, such as DNA and RNA.

These polynucleotides can be of any desired size that is effective to achieve the specificity desired. For example, a probe can be from about 7 or 8 nucleotides to several thousand nucleotides, depending upon its use and purpose. For instance, a probe used as a primer PCR can be shorter than a probe used in an ordered array of polynucleotide probes. Probe sizes vary, and the invention is not limited in any way by their size, e.g., probes can be from about 7-2000 nucleotides, 7-1000, 8-700, 8-600, 8-500, 8-400, 8-300, 8-150, 8-100, 8-75, 7-50, 10-25, 14-16, at least about 8, at least about 10, at least about 15, at least about 25, etc. The polynucleotides can have non-naturally-occurring nucleotides, e.g., inosine, AZT, 3TC, etc. The polynucleotides can have 100% sequence identity or complementarity to a sequence of Tables 1 and 2, or it can have mismatches or nucleotide substitutions, e.g., 1, 2, 3, 4, or 5 substitutions. The probes can be single-stranded or double-stranded.

In accordance with the present invention, a polynucleotide can be present in a kit, where the kit includes, e.g., one or more polynucleotides, a desired buffer (e.g., phosphate, tris, etc.), detection compositions, RNA or cDNA from different tissues to be used as controls, libraries, etc. The polynucleotide can be labeled or unlabeled, with radioactive or non-radioactive labels as known in the art. Kits can comprise one or more pairs of polynucleotides for amplifying nucleic acids specific for differentially-regulated genes of the present invention, e.g., comprising a forward and reverse primer effective in PCR. These include both sense and anti-sense orientations. For instance, in PCR-based methods (such as RT-PCR), a pair of primers are typically used, one having a sense sequence and the other having an antisense sequence.

Another aspect of the present invention is a nucleotide sequence that is specific to, or for, a selective polynucleotide. The phrases "specific for" or "specific to" a polynucleotide have a functional meaning that the polynucleotide can be used to identify the presence of one or more target genes in a sample. It is specific in the sense that it can be used to detect polynucleotides above background noise ("non-specific binding"). A specific sequence is a defined order of nucleotides which occurs in the polynucleotide, e.g., in the nucleotide sequences of Tables 1 and 2. A probe or mixture of probes can comprise a sequence or sequences that are specific to a plurality of target sequences, e.g., where the sequence is a consensus sequence, a functional domain, etc., e.g., capable of recognizing a family of related genes. Such sequences can be used as probes in any of the methods described herein or

incorporated by reference. Both sense and antisense nucleotide sequences are included. A specific polynucleotide according to the present invention can be determined routinely.

A polynucleotide comprising a specific sequence can be used as a hybridization probe to identify the presence of, e.g., human or mouse polynucleotide, in a sample comprising a mixture of polynucleotides, e.g., on a Northern blot. Hybridization can be performed under high stringent conditions (see, above) to select polynucleotides (and their complements which can contain the coding sequence) having at least 90%, 95%, 99%, etc., identity (i.e., complementarity) to the probe, but less stringent conditions can also be used. A specific polynucleotide sequence can also be fused in-frame, at either its 5' or 3' end, to various nucleotide sequences as mentioned throughout the patent, including coding sequences for enzymes, detectable markers, GFP, etc, expression control sequences, etc.

A polynucleotide probe, especially one that is specific to a polynucleotide of the present invention, can be used in gene detection and hybridization methods as already described. In one embodiment, a specific polynucleotide probe can be used to detect whether a particular tissue or cell-type is present in a target sample. To carry out such a method, a selective polynucleotide can be chosen which is characteristic of the desired target tissue. Such polynucleotide is preferably chosen so that it is expressed or displayed in the target tissue, but not in other tissues which are present in the sample. For instance, if detection of prostate is desired, it may not matter whether the selective polynucleotide is expressed in other tissues, as long as it is not expressed in cells normally present in blood, e.g., peripheral blood mononuclear cells. Starting from the selective polynucleotide, a specific polynucleotide probe can be designed which hybridizes (if hybridization is the basis of the assay) under the hybridization conditions to the selective polynucleotide, whereby the presence of the selective polynucleotide can be determined.

Probes which are specific for polynucleotides of the present invention can also be prepared using involve transcription-based systems, e.g., incorporating an RNA polymerase promoter into a selective polynucleotide of the present invention, and then transcribing anti-sense RNA using the polynucleotide as a template. See, e.g., U.S. Pat. No. 5,545,522.

### Polynucleotide composition

A polynucleotide according to the present invention can comprise, e.g., DNA, RNA, synthetic polynucleotide, peptide polynucleotide, modified nucleotides, dsDNA, ssDNA, ssRNA, dsRNA, and mixtures thereof. A polynucleotide can be single- or double-stranded,

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triplex, DNA:RNA, duplexes, comprise hairpins, and other secondary structures, etc.

Nucleotides comprising a polynucleotide can be joined via various known linkages, e.g., ester, sulfamate, sulfamide, phosphorothioate, phosphoramidate, methylphosphonate, carbamate, etc., depending on the desired purpose, e.g., resistance to nucleases, such as RNase H, improved in vivo stability, etc. See, e.g., U.S. Pat. No. 5,378,825. Any desired nucleotide or nucleotide analog can be incorporated, e.g., 6-mercaptoguanine, 8-oxo-guanine, etc.

Various modifications can be made to the polynucleotides, such as attaching detectable markers (avidin, biotin, radioactive elements, fluorescent tags and dyes, energy transfer labels, energy-emitting labels, binding partners, etc.) or moieties which improve hybridization, detection, and/or stability. The polynucleotides can also be attached to solid supports, e.g., nitrocellulose, magnetic or paramagnetic microspheres (e.g., as described in U.S. Pat. No. 5,411,863; U.S. Pat. No. 5,543,289; for instance, comprising ferromagnetic, supermagnetic, paramagnetic, superparamagnetic, iron oxide and polysaccharide), nylon, agarose, diazotized cellulose, latex solid microspheres, polyacrylamides, etc., according to a desired method. See, e.g., U.S. Pat. Nos. 5,470,967, 5,476,925, and 5,478,893.

Polynucleotide according to the present invention can be labeled according to any desired method. The polynucleotide can be labeled using radioactive tracers such as  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^3\text{H}$ , or  $^{14}\text{C}$ , to mention some commonly used tracers. The radioactive labeling can be carried out according to any method, such as, for example, terminal labeling at the 3' or 5' end using a radiolabeled nucleotide, polynucleotide kinase (with or without dephosphorylation with a phosphatase) or a ligase (depending on the end to be labeled). A non-radioactive labeling can also be used, combining a polynucleotide of the present invention with residues having immunological properties (antigens, haptens), a specific affinity for certain reagents (ligands), properties enabling detectable enzyme reactions to be completed (enzymes or coenzymes, enzyme substrates, or other substances involved in an enzymatic reaction), or characteristic physical properties, such as fluorescence or the emission or absorption of light at a desired wavelength, etc.

#### 30 Nucleic acid detection methods

Another aspect of the present invention relates to methods and processes for detecting differentially-regulated genes of the present invention. Detection methods have a variety of applications, including for diagnostic, prognostic, forensic, and research applications. To

accomplish gene detection, a polynucleotide in accordance with the present invention can be used as a "probe." The term "probe" or "polynucleotide probe" has its customary meaning in the art, e.g., a polynucleotide which is effective to identify (e.g., by hybridization), when used in an appropriate process, the presence of a target polynucleotide to which it is designed.

- 5 Identification can involve simply determining presence or absence, or it can be quantitative, e.g., in assessing amounts of a gene or gene transcript present in a sample. Probes can be useful in a variety of ways, such as for diagnostic purposes, to identify homologs, and to detect, quantitate, or isolate a polynucleotide of the present invention in a test sample.

- Assays can be utilized which permit quantification and/or presence/absence detection  
10 of a target nucleic acid in a sample. Assays can be performed at the single-cell level, or in a sample comprising many cells, where the assay is "averaging" expression over the entire collection of cells and tissue present in the sample. Any suitable assay format can be used, including, but not limited to, e.g., Southern blot analysis, Northern blot analysis, polymerase chain reaction ("PCR") (e.g., Saiki et al., *Science*, 241:53, 1988; U.S. Pat. Nos. 4,683,195,  
15 4,683,202, and 6,040,166; *PCR Protocols: A Guide to Methods and Applications*, Innis et al., eds., Academic Press, New York, 1990), reverse transcriptase polymerase chain reaction ("RT-PCR"), anchored PCR, rapid amplification of cDNA ends ("RACE") (e.g., Schaefer in *Gene Cloning and Analysis: Current Innovations*, Pages 99-115, 1997), ligase chain reaction ("LCR") (EP 320 308), one-sided PCR (Ohara et al., *Proc. Natl. Acad. Sci.*, 86:5673-5677,  
20 1989), indexing methods (e.g., U.S. Pat. No. 5,508,169), *in situ* hybridization, differential display (e.g., Liang et al., *Nucl. Acid. Res.*, 21:3269-3275, 1993; U.S. Pat. Nos. 5,262,311, 5,599,672 and 5,965,409; WO97/18454; Prashar and Weissman, *Proc. Natl. Acad. Sci.*, 93:659-663, and U.S. Pat. Nos. 6,010,850 and 5,712,126; Welsh et al., *Nucleic Acid Res.*, 20:4965-4970, 1992, and U.S. Pat. No. 5,487,985) and other RNA fingerprinting techniques,  
25 nucleic acid sequence based amplification ("NASBA") and other transcription based amplification systems (e.g., U.S. Pat. Nos. 5,409,818 and 5,554,527; WO 88/10315), polynucleotide arrays (e.g., U.S. Pat. Nos. 5,143,854, 5,424,186; 5,700,637, 5,874,219, and 6,054,270; PCT WO 92/10092; PCT WO 90/15070), Qbeta Replicase (PCT/US87/00880), Strand Displacement Amplification ("SDA"), Repair Chain Reaction ("RCR"), nuclease  
30 protection assays, subtraction-based methods, Rapid-Scan™, etc. Additional useful methods include, but are not limited to, e.g., template-based amplification methods, competitive PCR (e.g., U.S. Pat. No. 5,747,251), redox-based assays (e.g., U.S. Pat. No. 5,871,918), Taqman-based assays (e.g., Holland et al., *Proc. Natl. Acad. Sci.*, 88:7276-7280, 1991; U.S. Pat. Nos.

5,210,015 and 5,994,063), real-time fluorescence-based monitoring (e.g., U.S. Pat. 5,928,907), molecular energy transfer labels (e.g., U.S. Pat. Nos. 5,348,853, 5,532,129, 5,565,322, 6,030,787, and 6,117,635; Tyagi and Kramer, *Nature Biotech.*, 14:303-309, 1996). Any method suitable for single cell analysis of gene or protein expression can be  
5 used, including in situ hybridization, immunocytochemistry, MACS, FACS, flow cytometry, etc. For single cell assays, expression products can be measured using antibodies, PCR, or other types of nucleic acid amplification (e.g., Brady et al., *Methods Mol. & Cell. Biol.* 2, 17-25, 1990; Eberwine et al., 1992, *Proc. Natl. Acad. Sci.*, 89, 3010-3014, 1992; U.S. Pat. No. 5,723,290). These and other methods can be carried out conventionally, e.g., as described in  
10 the mentioned publications.

Many of such methods may require that the polynucleotide is labeled, or comprises a particular nucleotide type useful for detection. The present invention includes such modified polynucleotides that are necessary to carry out such methods. Thus, polynucleotides can be DNA, RNA, DNA:RNA hybrids, PNA, etc., and can comprise any modification or  
15 substituent which is effective to achieve detection.

Detection can be desirable for a variety of different purposes, including research, diagnostic, prognostic, and forensic. For diagnostic purposes, it may be desirable to identify the presence or quantity of a polynucleotide sequence in a sample, where the sample is obtained from tissue, cells, body fluids, etc. In a preferred method as described in more  
20 detail below, the present invention relates to a method of detecting a polynucleotide comprising, contacting a target polynucleotide in a test sample with a polynucleotide probe under conditions effective to achieve hybridization between the target and probe; and detecting hybridization.

Any test sample in which it is desired to identify a polynucleotide or polypeptide  
25 thereof can be used, including, e.g., blood, urine, saliva, stool (for extracting nucleic acid, see, e.g., U.S. Pat. No. 6,177,251), swabs comprising tissue, biopsied tissue, tissue sections, cultured cells, etc.

Detection can be accomplished in combination with polynucleotide probes for other genes, e.g., genes which are expressed in other disease states, tissues, cells, such as brain,  
30 heart, kidney, spleen, thymus, liver, stomach, small intestine, colon, muscle, lung, testis, placenta, pituitary, thyroid, skin, adrenal gland, pancreas, salivary gland, uterus, ovary, prostate gland, peripheral blood cells (T-cells, lymphocytes, etc.), embryo, normal breast fat,

adult and embryonic stem cells, specific cell-types, such as endothelial, epithelial, myocytes, adipose, luminal epithelial, basoepithelial, myoepithelial, stromal cells, etc.

Polynucleotides can be used in wide range of methods and compositions, including for detecting, diagnosing, staging, grading, assessing, prognosticating, etc. diseases and disorders associated with differentially-regulated genes of the present invention, for monitoring or assessing therapeutic and/or preventative measures, in ordered arrays, etc. Any method of detecting genes and polynucleotides of Tables 1 and 2 can be used; certainly, the present invention is not to be limited how such methods are implemented.

Along these lines, the present invention relates to methods of detecting differentially-regulated genes described herein in a sample comprising nucleic acid. Such methods can comprise one or more the following steps in any effective order, e.g., contacting said sample with a polynucleotide probe under conditions effective for said probe to hybridize specifically to nucleic acid in said sample, and detecting the presence or absence of probe hybridized to nucleic acid in said sample, wherein said probe is a polynucleotide which is Tables 1 and 2, a polynucleotide having, e.g., about 70%, 80%, 85%, 90%, 95%, 99%, or more sequence identity thereto, effective or specific fragments thereof, or complements thereto. The detection method can be applied to any sample, e.g., cultured primary, secondary, or established cell lines, tissue biopsy, blood, urine, stool, and other bodily fluids, for any purpose.

Contacting the sample with probe can be carried out by any effective means in any effective environment. It can be accomplished in a solid, liquid, frozen, gaseous, amorphous, solidified, coagulated, colloid, etc., mixtures thereof, matrix. For instance, a probe in an aqueous medium can be contacted with a sample which is also in an aqueous medium, or which is affixed to a solid matrix, or vice-versa.

Generally, as used throughout the specification, the term "effective conditions" means, e.g., the particular milieu in which the desired effect is achieved. Such a milieu, includes, e.g., appropriate buffers, oxidizing agents, reducing agents, pH, co-factors, temperature, ion concentrations, suitable age and/or stage of cell (such as, in particular part of the cell cycle, or at a particular stage where particular genes are being expressed) where cells are being used, culture conditions (including substrate, oxygen, carbon dioxide, etc.). When hybridization is the chosen means of achieving detection, the probe and sample can be combined such that the resulting conditions are functional for said probe to hybridize specifically to nucleic acid in said sample.



The phrase "hybridize specifically" indicates that the hybridization between single-stranded polynucleotides is based on nucleotide sequence complementarity. The effective conditions are selected such that the probe hybridizes to a preselected and/or definite target nucleic acid in the sample. For instance, if detection of a gene set forth in Tables 1 and 2 is desired, a probe can be selected which can hybridize to such target gene under high stringent conditions, without significant hybridization to other genes in the sample. To detect homologs of a gene set forth in Tables 1 and 2, the effective hybridization conditions can be less stringent, and/or the probe can comprise codon degeneracy, such that a homolog is detected in the sample.

As already mentioned, the methods can be carried out by any effective process, e.g., by Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, *in situ* hybridization, etc., as indicated above. When PCR based techniques are used, two or more probes are generally used. One probe can be specific for a defined sequence which is characteristic of a selective polynucleotide, but the other probe can be specific for the selective polynucleotide, or specific for a more general sequence, e.g., a sequence such as polyA which is characteristic of mRNA, a sequence which is specific for a promoter, ribosome binding site, or other transcriptional features, a consensus sequence (e.g., representing a functional domain). For the former aspects, 5' and 3' probes (e.g., polyA, Kozak, etc.) are preferred which are capable of specifically hybridizing to the ends of transcripts. When PCR is utilized, the probes can also be referred to as "primers" in that they can prime a DNA polymerase reaction.

In addition to testing for the presence or absence of polynucleotides, the present invention also relates to determining the amounts at which polynucleotides of the present invention are expressed in sample and determining the differential expression of such polynucleotides in samples.. Such methods can involve substantially the same steps as described above for presence/absence detection, e.g., contacting with probe, hybridizing, and detecting hybridized probe, but using more quantitative methods and/or comparisons to standards.

The amount of hybridization between the probe and target can be determined by any suitable methods, e.g., PCR, RT-PCR, RACE PCR, Northern blot, polynucleotide microarrays, Rapid-Scan, etc., and includes both quantitative and qualitative measurements. For further details, see the hybridization methods described above and below. Determining by such hybridization whether the target is differentially expressed (e.g., up-regulated or

differentially-regulated) in the sample can also be accomplished by any effective means. For instance, the target's expression pattern in the sample can be compared to its pattern in a known standard, such as in a normal tissue, or it can be compared to another gene in the same sample. When a second sample is utilized for the comparison, it can be a sample of normal  
5 tissue that is known not to contain diseased cells. The comparison can be performed on samples which contain the same amount of RNA (such as polyadenylated RNA or total RNA), or, on RNA extracted from the same amounts of starting tissue. Such a second sample can also be referred to as a control or standard. Hybridization can also be compared to a second target in the same tissue sample. Experiments can be performed that determine a  
10 ratio between the target nucleic acid and a second nucleic acid (a standard or control) , e.g., in a normal tissue. When the ratio between the target and control are substantially the same in a normal and sample, the sample is determined or diagnosed not to contain cells. However, if the ratio is different between the normal and sample tissues, the sample is determined to contain cancer cells. The approaches can be combined, and one or more second samples, or  
15 second targets can be used. Any second target nucleic acid can be used as a comparison, including "housekeeping" genes, such as beta-actin, alcohol dehydrogenase, or any other gene whose expression does not vary depending upon the disease status of the cell.

Methods of identifying polymorphisms, mutations, etc., of a differentially-regulated gene  
20 Polynucleotides of the present invention can also be utilized to identify mutant alleles, SNPs, gene rearrangements and modifications, and other polymorphisms of the wild-type gene. Mutant alleles, polymorphisms, SNPs, etc., can be identified and isolated from cancers that are known, or suspected to have, a genetic component. Identification of such genes can be carried out routinely (see, above for more guidance), e.g., using PCR, hybridization  
25 techniques, direct sequencing, mismatch reactions (see, e.g., above), RFLP analysis, SSCP (e.g., Orita et al., *Proc. Natl. Acad. Sci.*, 86:2766, 1992), etc., where a polynucleotide having a sequence selected from Tables 1 and 2 is used as a probe, or genomic sequences thereof. The selected mutant alleles, SNPs, polymorphisms, etc., can be used diagnostically to determine whether a subject has, or is susceptible to a disorder associated with a  
30 differentially-regulated gene, as well as to design therapies and predict the outcome of the disorder. Methods involve, e.g., diagnosing a disorder associated with a differentially-regulated gene or determining susceptibility to a disorder, comprising, detecting the presence of a mutation in a gene selected from Tables 1 and 2. The detecting can be carried out by any

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effective method, e.g., obtaining cells from a subject, determining the gene sequence or structure of a target gene (using, e.g., mRNA, cDNA, genomic DNA, etc), comparing the sequence or structure of the target gene to the structure of the normal gene, whereby a difference in sequence or structure indicates a mutation in the gene in the subject.

- 5 Polynucleotides can also be used to test for mutations, SNPs, polymorphisms, etc., e.g., using mismatch DNA repair technology as described in U.S. Pat. No. 5,683,877; U.S. Pat. No. 5,656,430; Wu et al., *Proc. Natl. Acad. Sci.*, 89:8779-8783, 1992.

The present invention also relates to methods of detecting polymorphisms in a differentially-regulated gene, comprising, e.g., comparing the structure of: genomic DNA  
10 comprising all or part of said gene, mRNA comprising all or part of said gene, cDNA comprising all or part of said gene, or a polypeptide comprising all or part of said gene, with the structure of said gene as set forth herein. The methods can be carried out on a sample from any source, e.g., cells, tissues, body fluids, blood, urine, stool, hair, egg, sperm, etc.

- 15 These methods can be implemented in many different ways. For example, "comparing the structure" steps include, but are not limited to, comparing restriction maps, nucleotide sequences, amino acid sequences, RFLPs, DNase sites, DNA methylation fingerprints (e.g., U.S. Pat. No. 6,214,556), protein cleavage sites, molecular weights, electrophoretic mobilities, charges, ion mobility, etc., between a standard gene  
20 and a test gene. The term "structure" can refer to any physical characteristics or configurations which can be used to distinguish between nucleic acids and polypeptides. The methods and instruments used to accomplish the comparing step depends upon the physical characteristics which are to be compared. Thus, various techniques are contemplated, including, e.g., sequencing machines (both amino acid and polynucleotide),  
25 electrophoresis, mass spectrometer (U.S. Pat. Nos. 6,093,541, 6,002,127), liquid chromatography, HPLC, etc.

- To carry out such methods, "all or part" of the gene or polypeptide can be compared. For example, if nucleotide sequencing is utilized, the entire gene can be sequenced, including promoter, introns, and exons, or only parts of it can be sequenced  
30 and compared, e.g., exon 1, exon 2, etc.

#### Mutagenesis

Mutated polynucleotide sequences of the present invention are useful for various

purposes, e.g., to create mutations of the polypeptides they encode, to identify functional regions of genomic DNA, to produce probes for screening libraries, etc. Mutagenesis can be carried out routinely according to any effective method, e.g., oligonucleotide-directed (Smith, M., *Ann. Rev. Genet.* 19:423-463, 1985), degenerate oligonucleotide-directed (Hill et al.,  
5 *Method Enzymology*, 155:558-568, 1987), region-specific (Myers et al., *Science*, 229:242-246, 1985; Derbyshire et al., *Gene*, 46:145, 1986; Ner et al., *DNA*, 7:127, 1988), linker-scanning (McKnight and Kingsbury, *Science*, 217:316-324, 1982), directed using PCR, recursive ensemble mutagenesis (Arkin and Yourvan, *Proc. Natl. Acad. Sci.*, 89:7811-7815, 1992), random mutagenesis (e.g., U.S. Pat. Nos. 5,096,815; 5,198,346; and 5,223,409), site-  
10 directed mutagenesis (e.g., Walder et al., *Gene*, 42:133, 1986; Bauer et al., *Gene*, 37:73, 1985; Craik, *Bio Techniques*, January 1985, 12-19; Smith et al., *Genetic Engineering: Principles and Methods*, Plenum Press, 1981), phage display (e.g., Lowman et al., *Biochem.* 30:10832-10837, 1991; Ladner et al., U.S. Pat. No. 5,223,409; Huse, WIPO Publication WO 92/06204), etc. Desired sequences can also be produced by the assembly of target sequences  
15 using mutually priming oligonucleotides (Uhlmann, *Gene*, 71:29-40, 1988). For directed mutagenesis methods, analysis of the three-dimensional structure of a polypeptide can be used to guide and facilitate making mutants which effect polypeptide activity. Sites of substrate-enzyme interaction or other biological activities can also be determined by analysis of crystal structure as determined by such techniques as nuclear magnetic resonance,  
20 crystallography or photoaffinity labeling. See, for example, de Vos et al., *Science* 255:306-312, 1992; Smith et al., *J. Mol. Biol.* 224:899-904, 1992; Wlodaver et al., *FEBS Lett.* 309:59-64, 1992.

In addition, libraries of differentially-regulated genes and fragments thereof can be used for screening and selection of gene variants. For instance, a library of coding sequences  
25 can be generated by treating a double-stranded DNA with a nuclease under conditions where the nicking occurs, e.g., only once per molecule, denaturing the double-stranded DNA, renaturing it to for double-stranded DNA that can include sense/antisense pairs from different nicked products, removing single-stranded portions from reformed duplexes by treatment with S1 nuclease, and ligating the resulting DNAs into an expression vecore. By this  
30 method, expression libraries can be made comprising "mutagenized" differentially-regulated genes. The entire coding sequence or parts thereof can be used.

Polynucleotide expression, polypeptides produced thereby, and specific-binding partners thereto.

A polynucleotide according to the present invention can be expressed in a variety of different systems, in vitro and in vivo, according to the desired purpose. For example, a  
5 polynucleotide can be inserted into an expression vector, introduced into a desired host, and cultured under conditions effective to achieve expression of a polypeptide coded for by the polynucleotide, to search for specific binding partners. Effective conditions include any culture conditions which are suitable for achieving production of the polypeptide by the host cell, including effective temperatures, pH, medium, additives to the media in which the host  
10 cell is cultured (e.g., additives which amplify or induce expression such as butyrate, or methotrexate if the coding polynucleotide is adjacent to a dhfr gene), cycloheximide, cell densities, culture dishes, etc. A polynucleotide can be introduced into the cell by any effective method including, e.g., naked DNA, calcium phosphate precipitation, electroporation, injection, DEAE-Dextran mediated transfection, fusion with liposomes,  
15 association with agents which enhance its uptake into cells, viral transfection. A cell into which a polynucleotide of the present invention has been introduced is a transformed host cell. The polynucleotide can be extrachromosomal or integrated into a chromosome(s) of the host cell. It can be stable or transient. An expression vector is selected for its compatibility with the host cell. Host cells include, mammalian cells, e.g., COS, CV1, BHK, CHO, HeLa,  
20 LTK, NIH 3T3, PC-3 (CRL-1435), LNCaP (CRL-1740), CA-HPV-10 (CRL-2220), PZ-HPV-7 (CRL-2221), MDA-PCa 2b (CRL-2422), 22Rv1 (CRL2505), NCI-H660 (CRL-5813), HS 804.Sk (CRL-7535), LNCaP-FGF (CRL-10995), RWPE-1 (CRL-11609), RWPE-2 (CRL-11610), PWR-1E (CRL 11611), rat MAT-Ly-LuB-2 (CRL-2376), and other prostate cells, insect cells, such as Sf9 (*S. frugipeda*) and *Drosophila*, bacteria, such as  
25 *E. coli*, *Streptococcus*, *Bacillus*, yeast, such as *Sacharomyces*, *S. cerevisiae*, fungal cells, plant cells, embryonic or adult stem cells (e.g., mammalian, such as mouse or human).

Expression control sequences are similarly selected for host compatibility and a desired purpose, e.g., high copy number, high amounts, induction, amplification, controlled expression. Other sequences which can be employed include enhancers such as from SV40,  
30 CMV, RSV, inducible promoters, cell-type specific elements, or sequences which allow selective or specific cell expression. Promoters that can be used to drive its expression, include, e.g., the endogenous promoter, MMTV, SV40, trp, lac, tac, or T7 promoters for bacterial hosts; or alpha factor, alcohol oxidase, or PGH promoters for yeast. RNA

promoters can be used to produced RNA transcripts, such as T7 or SP6. See, e.g., Melton et al., *Polynucleotide Res.*, 12(18):7035-7056, 1984; Dunn and Studier. *J. Mol. Bio.*, 166:477-435, 1984; U.S. Pat. No. 5,891,636; Studier et al., *Gene Expression Technology, Methods in Enzymology*, 85:60-89, 1987. In addition, as discussed above, translational signals (including in-frame insertions) can be included.

When a polynucleotide is expressed as a heterologous gene in a transfected cell line, the gene is introduced into a cell as described above, under effective conditions in which the gene is expressed. The term "heterologous" means that the gene has been introduced into the cell line by the "hand-of-man." Introduction of a gene into a cell line is discussed above.

10 The transfected (or transformed) cell expressing the gene can be lysed or the cell line can be used intact.

For expression and other purposes, a polynucleotide can contain codons found in a naturally-occurring gene, transcript, or cDNA, for example, e.g., as set forth in Tables 1 and 2, or it can contain degenerate codons coding for the same amino acid sequences. For instance, it may be desirable to change the codons in the sequence to optimize the sequence for expression in a desired host. See, e.g., U.S. Pat. Nos. 5,567,600 and 5,567,862.

A polypeptide according to the present invention can be recovered from natural sources, transformed host cells (culture medium or cells) according to the usual methods, including, detergent extraction (e.g., non-ionic detergent, Triton X-100, CHAPS, octylglucoside, Igepal CA-630), ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, hydroxyapatite chromatography, lectin chromatography, gel electrophoresis. Protein refolding steps can be used, as necessary, in completing the configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for purification steps. Another approach is express the polypeptide recombinantly with an affinity tag (Flag epitope, HA epitope, myc epitope, 6xHis, maltose binding protein, chitinase, etc) and then purify by anti-tag antibody-conjugated affinity chromatography.

The present invention also relates to antibodies, and other specific-binding partners, which are specific for polypeptides encoded by polynucleotides of the present invention. Antibodies, e.g., polyclonal, monoclonal, recombinant, chimeric, humanized, single-chain, Fab, and fragments thereof, can be prepared according to any desired method. See, also, screening recombinant immunoglobulin libraries (e.g., Orlandi et al., *Proc. Natl. Acad. Sci.*,

86:3833-3837, 1989; Huse et al., *Science*, 256:1275-1281, 1989); in vitro stimulation of lymphocyte populations; Winter and Milstein, *Nature*, 349: 293-299, 1991. The antibodies can be IgM, IgG, subtypes, IgG2a, IgG1, etc. Antibodies, and immune responses, can also be generated by administering naked DNA See, e.g., U.S. Pat. Nos. 5,703,055; 5,589,466; 5,580,859. Antibodies can be used from any source, including, goat, rabbit, mouse, chicken (e.g., IgY; see, Duan, W0/029444 for methods of making antibodies in avian hosts, and harvesting the antibodies from the eggs). An antibody specific for a polypeptide means that the antibody recognizes a defined sequence of amino acids within or including the polypeptide. Other specific binding partners include, e.g., aptamers and PNA, can be prepared against specific epitopes or domains of differentially regulated genes.

The preparation of polyclonal antibodies is well-known to those skilled in the art. See, for example, Green et al., Production of Polyclonal Antisera, in IMMUNOCHEMICAL PROTOCOLS (Manson, ed.), pages 1-5 (Humana Press 1992); Coligan et al., Production of Polyclonal Antisera in Rabbits, Rats, Mice and Hamsters, in CURRENT PROTOCOLS IN IMMUNOLOGY, section 2.4.1 (1992). The preparation of monoclonal antibodies likewise is conventional. See, for example, Kohler & Milstein, *Nature* 256:495 (1975); Coligan et al., sections 2.5.1-2.6.7; and Harlow et al., ANTIBODIES: A LABORATORY MANUAL, page 726 (Cold Spring Harbor Pub. 1988).

Antibodies can also be humanized, e.g., where they are to be used therapeutically. Humanized monoclonal antibodies are produced by transferring mouse complementarity determining regions from heavy and light variable chains of the mouse immunoglobulin into a human variable domain, and then substituting human residues in the framework regions of the murine counterparts. The use of antibody components derived from humanized monoclonal antibodies obviates potential problems associated with the immunogenicity of murine constant regions. General techniques for cloning murine immunoglobulin variable domains are described, for example, by Orlandi et al., *Proc. Nat'l Acad. Sci. USA* 86:3833 (1989), which is hereby incorporated in its entirety by reference. Techniques for producing humanized monoclonal antibodies are described, for example, in U.S. Pat. No. 6,054,297, Jones et al., *Nature* 321: 522 (1986); Riechmann et al., *Nature* 332: 323 (1988); Verhoeyen et al., *Science* 239: 1534 (1988); Carter et al., *Proc. Nat'l Acad. Sci. USA* 89: 4285 (1992); Sandhu, *Crit. Rev. Biotech.* 12: 437 (1992); and Singer et al., *J. Immunol.* 150: 2844 (1993).

Antibodies of the invention also may be derived from human antibody fragments isolated from a combinatorial immunoglobulin library. See, for example, Barbas et al.,

METHODS: A COMPANION TO METHODS IN ENZYMOLOGY, VOL. 2, page 119 (1991); Winter et al., *Ann. Rev. Immunol.* 12: 433 (1994). Cloning and expression vectors that are useful for producing a human immunoglobulin phage library can be obtained commercially, for example, from STRATAGENE Cloning Systems (La Jolla, Calif.).

5           In addition, antibodies of the present invention may be derived from a human monoclonal antibody. Such antibodies are obtained from transgenic mice that have been "engineered" to produce specific human antibodies in response to antigenic challenge. In this technique, elements of the human heavy and light chain loci are introduced into strains of mice derived from embryonic stem cell lines that contain targeted disruptions of the  
10   endogenous heavy and light chain loci. The transgenic mice can synthesize human antibodies specific for human antigens and can be used to produce human antibody-secreting hybridomas. Methods for obtaining human antibodies from transgenic mice are described, e.g., in Green et al., *Nature Genet.* 7:13 (1994); Lonberg et al., *Nature* 368:856 (1994); and Taylor et al., *Int. Immunol.* 6:579 (1994).

15           Antibody fragments of the present invention can be prepared by proteolytic hydrolysis of the antibody or by expression in *E. coli* of nucleic acid encoding the fragment. Antibody fragments can be obtained by pepsin or papain digestion of whole antibodies by conventional methods. For example, antibody fragments can be produced by enzymatic cleavage of antibodies with pepsin to provide a 5S fragment denoted F(ab')<sub>2</sub>. This fragment can be  
20   further cleaved using a thiol reducing agent, and optionally a blocking group for the sulfhydryl groups resulting from cleavage of disulfide linkages, to produce 3.5S Fab' monovalent fragments. Alternatively, an enzymatic cleavage using pepsin produces two monovalent Fab' fragments and an Fc fragment directly. These methods are described, for example, by Goldenberg, U.S. Pat. No. 4,036,945 and No. 4,331,647, and references  
25   contained therein. These patents are hereby incorporated in their entireties by reference. See also Nisoihoff et al., *Arch. Biochem. Biophys.* 89:230 (1960); Porter, *Biochem. J.* 73:119 (1959); Edelman et al., *METHODS IN ENZYMOLOGY*, VOL. 1, page 422 (Academic Press 1967); and Coligan et al. at sections 2.8.1-2.8.10 and 2.10.1-2.10.4.

30           Other methods of cleaving antibodies, such as separation of heavy chains to form monovalent light-heavy chain fragments, further cleavage of fragments, or other enzymatic, chemical, or genetic techniques can also be used. For example, Fv fragments comprise an association of V<sub>H</sub> and V<sub>L</sub> chains. This association may be noncovalent, as described in Inbar et al., *Proc. Nat'l Acad. Sci. USA* 69:2659 (1972). Alternatively, the



variable chains can be linked by an intermolecular disulfide bond or cross-linked by chemicals such as glutaraldehyde. See, e.g., Sandhu, *supra*. Preferably, the Fv fragments comprise V.sub.H and V.sub.L chains connected by a peptide linker. These single-chain antigen binding proteins (sFv) are prepared by constructing a structural gene comprising

5 nucleic acid sequences encoding the V.sub.H and V.sub.L domains connected by an oligonucleotide. The structural gene is inserted into an expression vector, which is subsequently introduced into a host cell such as *E. coli*. The recombinant host cells synthesize a single polypeptide chain with a linker peptide bridging the two V domains. Methods for producing sFvs are described, for example, by Whitlow et al., METHODS: A

10 COMPANION TO METHODS IN ENZYMOLOGY, VOL. 2, page 97 (1991); Bird et al., Science 242:423-426 (1988); Ladner et al., U.S. Pat. No. 4,946,778; Pack et al., Bio/Technology 11: 1271-77 (1993); and Sandhu, *supra*.

Another form of an antibody fragment is a peptide coding for a single complementarity-determining region (CDR). CDR peptides ("minimal recognition units") can

15 be obtained by constructing genes encoding the CDR of an antibody of interest. Such genes are prepared, for example, by using the polymerase chain reaction to synthesize the variable region from RNA of antibody-producing cells. See, for example, Larrick et al., METHODS: A COMPANION TO METHODS IN ENZYMOLOGY, VOL. 2, page 106 (1991).

The term "antibody" as used herein includes intact molecules as well as fragments

20 thereof, such as Fab, F(ab')<sub>2</sub>, and Fv which are capable of binding to an epitopic determinant present in Bin1 polypeptide. Such antibody fragments retain some ability to selectively bind with its antigen or receptor. The term "epitope" refers to an antigenic determinant on an antigen to which the paratope of an antibody binds. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains

25 and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Antibodies can be prepared against specific epitopes or polypeptide domains.

Antibodies which bind to a differentially-regulated polypeptide of the present invention can be prepared using an intact polypeptide or fragments containing small peptides

30 of interest as the immunizing antigen. For example, it may be desirable to produce antibodies that specifically bind to the N- or C-terminal domains of said polypeptide. The polypeptide or peptide used to immunize an animal which is derived from translated cDNA or chemically synthesized which can be conjugated to a carrier protein, if desired. Such commonly used

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carriers which are chemically coupled to the immunizing peptide include keyhole limpet hemocyanin (KLH), thyroglobulin, bovine serum albumin (BSA), and tetanus toxoid.

Polyclonal or monoclonal antibodies can be further purified, for example, by binding to and elution from a matrix to which the polypeptide or a peptide to which the antibodies were raised is bound. Those of skill in the art will know of various techniques common in the immunology arts for purification and/or concentration of polyclonal antibodies, as well as monoclonal antibodies (See for example, Coligan, et al., Unit 9, *Current Protocols in Immunology*, Wiley Interscience, 1994, incorporated by reference).

Anti-idiotypic technology can also be used to produce invention monoclonal antibodies which mimic an epitope. For example, an anti-idiotypic monoclonal antibody made to a first monoclonal antibody will have a binding domain in the hypervariable region which is the "image" of the epitope bound by the first monoclonal antibody.

#### Methods of detecting polypeptides

Polypeptides coded for by a differentially-regulated gene of the present invention can be detected, visualized, determined, quantitated, etc. according to any effective method. useful methods include, e.g., but are not limited to, immunoassays, RIA (radioimmunoassay), ELISA, (enzyme-linked-immunosorbent assay), immunofluorescence, flow cytometry, histology, electron microscopy, light microscopy, in situ assays, immunoprecipitation, Western blot, etc.

Immunoassays may be carried in liquid or on biological support. For instance, a sample (e.g., blood, stool, urine, cells, tissue, body fluids, etc.) can be brought in contact with and immobilized onto a solid phase support or carrier such as nitrocellulose, or other solid support that is capable of immobilizing cells, cell particles or soluble proteins. The support may then be washed with suitable buffers followed by treatment with the detectably labeled differentially-regulated gene specific antibody. The solid phase support can then be washed with a buffer a second time to remove unbound antibody. The amount of bound label on solid support may then be detected by conventional means.

A "solid phase support or carrier" includes any support capable of binding an antigen, antibody, or other specific binding partner. Supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, and magnetite. A support material can have any structural or physical configuration. Thus, the support configuration may be spherical, as in a bead, or cylindrical,

as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc. Preferred supports include polystyrene beads

One of the many ways in which gene peptide-specific antibody can be detectably  
5 labeled is by linking it to an enzyme and using it in an enzyme immunoassay (EIA). See, e.g., Voller, A., "The Enzyme Linked Immunosorbent Assay (ELISA)," 1978, Diagnostic Horizons 2, 1-7, Microbiological Associates Quarterly Publication, Walkersville, Md.); Voller, A. et al., 1978, J. Clin. Pathol. 31, 507-520; Butler, J. E., 1981, Meth. Enzymol. 73, 482-523; Maggio, E. (ed.), 1980, Enzyme Immunoassay, CRC Press, Boca Raton, Fla.. The  
10 enzyme which is bound to the antibody will react with an appropriate substrate, preferably a chromogenic substrate, in such a manner as to produce a chemical moiety that can be detected, for example, by spectrophotometric, fluorimetric or by visual means. Enzymes that can be used to detectably label the antibody include, but are not limited to, malate dehydrogenase, staphylococcal nuclease, delta-5-steroid isomerase, yeast alcohol  
15 dehydrogenase, .alpha.-glycerophosphate, dehydrogenase, triose phosphate isomerase, horseradish peroxidase, alkaline phosphatase, asparaginase, glucose oxidase, .beta.-galactosidase, ribonuclease, urease, catalase, glucose-6-phosphate dehydrogenase, glucoamylase and acetylcholinesterase. The detection can be accomplished by colorimetric methods that employ a chromogenic substrate for the enzyme. Detection may also be  
20 accomplished by visual comparison of the extent of enzymatic reaction of a substrate in comparison with similarly prepared standards.

Detection may also be accomplished using any of a variety of other immunoassays. For example, by radioactively labeling the antibodies or antibody fragments, it is possible to detect differentially-regulated peptides through the use of a radioimmunoassay (RIA). See,  
25 e.g., Weintraub, B., Principles of Radioimmunoassays, Seventh Training Course on Radioligand Assay Techniques, The Endocrine Society, March, 1986. The radioactive isotope can be detected by such means as the use of a gamma counter or a scintillation counter or by autoradiography.

It is also possible to label the antibody with a fluorescent compound. When the  
30 fluorescently labeled antibody is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, o-phthaldehyde and fluorescamine. The antibody can also be detectably

labeled using fluorescence emitting metals such as those in the lanthanide series. These metals can be attached to the antibody using such metal chelating groups as diethylenetriaminepentacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).

5 The antibody also can be detectably labeled by coupling it to a chemiluminescent compound. The presence of the chemiluminescent-tagged antibody is then determined by detecting the presence of luminescence that arises during the course of a chemical reaction. Examples of useful chemiluminescent labeling compounds are luminol, isoluminol, theromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

10 Likewise, a bioluminescent compound may be used to label the antibody of the present invention. Bioluminescence is a type of chemiluminescence found in biological systems in which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of luminescence. Important bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

15

#### Tissue and Disease

The prostate is a secretory organ surrounding the neck of the bladder and urethra. Its primary function is to produce fluids and other materials necessary for sperm transport and maintenance. Structurally, it has both glandular and nonglandular components. The glandular component is predominantly comprised of ducts and acini responsible for the production and transport prostatic fluids. Epithelial cells are the main identifiable cell found in these regions, primarily of the basal and secretory types, but also endocrine-paracrine and transitional epithelial. The non-glandular component contains the capsular and muscle tissues, which, respectively, hold the organ together and function in fluid discharge. See, 20 e.g., Histology for Pathologists, Sternberg, S.S., editor, Raven Press, NY, 1992, Chapter 40.

25 The major diseases of the prostate include, e.g., prostatic hyperplasia (BPH), prostatitis, and prostate cancer (e.g., prostatic adenocarcinoma). BPH is a benign, proliferative disease of the prostatic epithelial cells. While it may cause urinary tract obstruction in some patients, for the most part, it is generally asymptomatic. Prostate cancer, 30 on the other hand, is the most common form of cancer in white males in the United States, occurring predominantly in males over age 50. The prevalence of prostate diseases, such as prostate cancer, has made the discovery of prostate selective markers and gene expression patterns of great importance.

The most common scale of assessing prostate pathology is the Gleason grading system. See, e.g., Bostwick, *Am. J. Clin. Path.*, 102: s38-s56, 1994. Once the cancer is identified, staging can assess the size, location, and extent of the cancer. Several different staging scales are commonly used, including stages A-D, and Tumor-Nodes-Metastases (TNM). For treatment, diagnosis, staging, etc., of prostate conditions, methods can be carried out analogously to, and in combination with, U.S. Pat. Nos. 6,107,090; 6,057,116; 6,034,218; 6,004,267; 5,919,638; 5,882,864; 5,763,202; 5,747,264; 5,688,649; 5,552,277.

In addition, the present invention relates to methods of assessing a therapeutic or preventative intervention in a subject having a prostate cancer, comprising, e.g., detecting the expression levels of differentially-regulated target genes, wherein the target genes comprise a gene which is represented by a sequence selected from Tables 1 and 2, or, a gene represented by a sequence having 95% sequence identity or more to a sequence selected from Tables 1 and 2. By "therapeutic or preventative intervention," it is meant, e.g., a drug administered a patient, surgery, radiation, chemotherapy, and other measures taken to prevent a cancer or treat a cancer.

#### Grading, staging, comparing, assessing, methods and compositions

The present invention also relates to methods and compositions for staging and grading cancers. As already defined, staging relates to determining the extent of a cancer's spread, including its size and the degree to which other tissues, such as lymph nodes are involved in the cancer. Grading refers to the degree of a cell's retention of the characteristics of the tissue of its origin. A lower grade cancer comprises tumor cells that more closely resemble normal cells than a medium or higher grade cancer. Grading can be a useful diagnostic and prognostic tool. Higher grade cancers usually behave more aggressively than lower grade cancers. Thus, knowledge of the cancer grade, as well as its stage, can be a significant factor in the choice of the appropriate therapeutic intervention for the particular patient, e.g., surgery, radiation, chemotherapy, etc. Staging and grading can also be used in conjunction with a therapy to assess its efficacy, to determine prognosis, to determine effective dosages, etc.

Various methods of staging and grading cancers can be employed in accordance with the present invention. A "cell expression profile" or "cell expression fingerprint" is a representation of the expression of various different genes (e.g., polynucleotide sequences of SEQ ID NOS 1-107) in a given cell or sample comprising cells. These cell expression

profiles can be useful as reference standards. The cell expression fingerprints can be used alone for grading, or in combination with other grading methods.

The present invention also relates to methods and compositions for diagnosing a prostate cancer, or determining susceptibility to a prostate cancer, using polynucleotides, polypeptides, and specific-binding partners of the present invention to detect, assess, 5 determine, etc., differentially-regulated genes of the present invention. In such methods, the gene can serve as a marker for prostate cancer, e.g., where the gene, when mutant, is a direct cause of the prostate cancer; where the gene is affected by another gene(s) which is directly responsible for the prostate cancer, e.g., when the gene is part of the same signaling pathway 10 as the directly responsible gene; and, where the gene is chromosomally linked to the gene(s) directly responsible for the prostate cancer, and segregates with it. Many other situations are possible. To detect, assess, determine, etc., a probe specific for the gene can be employed as described above and below. Any method of detecting and/or assessing the gene can be used, including detecting expression of the gene using polynucleotides, antibodies, or other 15 specific-binding partners.

The present invention relates to methods of diagnosing a disorder associated with prostate cancer, or determining a subject's susceptibility to such prostate cancer, comprising, e.g., assessing the expression of a differentially-regulated gene in a tissue sample comprising tissue or cells suspected of having prostate cancer (e.g., where the sample 20 comprises prostate). The phrase "diagnosing" indicates that it is determined whether the sample has a prostate cancer cells. "Determining a subject's susceptibility to a prostate cancer" indicates that the subject is assessed for whether s/he is predisposed to get such a disease or disorder, where the predisposition is indicated by abnormal expression of the gene (e.g., gene mutation, gene expression pattern is not normal, etc.). Predisposition or 25 susceptibility to a disease may result when a such disease is influenced by epigenetic, environmental, etc., factors.

By the phrase "assessing expression of a differentially-regulated gene," it is meant that the functional status of the gene is evaluated. This includes, but is not limited to, measuring expression levels of said gene, determining the genomic structure of said gene, 30 determining the mRNA structure of transcripts from said gene, or measuring the expression levels of polypeptide coded for by said gene. Thus, the term "assessing expression" includes evaluating the all aspects of the transcriptional and translational machinery of the gene. For instance, if a promoter defect causes, or is suspected of

causing, the disorder, then a sample can be evaluated (i.e., "assessed") by looking (e.g., sequencing or restriction mapping) at the promoter sequence in the gene, by detecting transcription products (e.g., RNA), by detecting translation product (e.g., polypeptide). Any measure of whether the gene is functional can be used, including, polypeptide, polynucleotide, and functional assays for the gene's biological activity.

In making the assessment, it can be useful to compare the results to a normal gene, e.g., a gene which is not associated with the disorder. The nature of the comparison can be determined routinely, depending upon how the assessing is accomplished. If, for example, the mRNA levels of a sample is detected, then the mRNA levels of a normal can serve as a comparison, or a gene which is known not to be affected by the disorder. Methods of detecting mRNA are well known, and discussed above, e.g., but not limited to, Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, etc. Similarly, if polypeptide production is used to evaluate the gene, then the polypeptide in a normal tissue sample can be used as a comparison, or, polypeptide from a different gene whose expression is known not to be affected by the disorder. These are only examples of how such a method could be carried out.

Assessing the effects of therapeutic and preventative interventions (e.g., administration of a drug, chemotherapy, radiation, etc.) on prostate cancer is a major effort in drug discovery, clinical medicine, and pharmacogenomics. The evaluation of therapeutic and preventative measures, whether experimental or already in clinical use, has broad applicability, e.g., in clinical trials, for monitoring the status of a patient, for analyzing and assessing animal models, and in any scenario involving cancer treatment and prevention. Analyzing the expression profiles of polynucleotides of the present invention can be utilized as a parameter by which interventions are judged and measured. Treatment of a disorder can change the expression profile in some manner which is prognostic or indicative of the drug's effect on it. Changes in the profile can indicate, e.g., drug toxicity, return to a normal level, etc. Accordingly, the present invention also relates to methods of monitoring or assessing a therapeutic or preventative measure (e.g., chemotherapy, radiation, anti-neoplastic drugs, antibodies, etc.) in a subject having prostate cancer, or, susceptible to such a disorder, comprising, e.g., detecting the expression levels of one or more differentially-regulated genes of the present invention. A subject can be a cell-based assay system, non-human animal model, human patient, etc. Detecting can be accomplished as described for the methods above and below. By

“therapeutic or preventative intervention,” it is meant, e.g., a drug administered to a patient, surgery, radiation, chemotherapy, and other measures taken to prevent, treat, or diagnose prostate cancer.

5 Expression can be assessed in any sample comprising any tissue or cell type, body fluid, etc., as discussed for other methods of the present invention, including cells from prostate can be used, or cells derived from prostate. By the phrase “cells derived from prostate,” it is meant that the derived cells originate from prostate, e.g., when metastasis from a primary tumor site has occurred, when a progenitor-type or pluripotent cell gives rise to other cells, etc.

10

#### Identifying agent methods

The present invention also relates to methods of identifying agents, and the agents themselves, which modulate prostate cancer genes. These agents can be used to modulate the biological activity of the polypeptide encoded for the gene, or the gene, itself. Agents which  
15 regulate the gene or its product are useful in variety of different environments, including as medicinal agents to treat or prevent disorders associated with prostate cancer genes and as research reagents to modify the function of tissues and cell.

Methods of identifying agents generally comprise steps in which an agent is placed in contact with the gene, transcription product, translation product, or other target, and then a  
20 determination is performed to assess whether the agent “modulates” the target. The specific method utilized will depend upon a number of factors, including, e.g., the target (i.e., is it the gene or polypeptide encoded by it), the environment (e.g., in vitro or in vivo), the composition of the agent, etc.

For modulating the expression of a prostate cancer gene, a method can comprise, in  
25 any effective order, one or more of the following steps, e.g., contacting a prostate cancer gene (e.g., in a cell population) with a test agent under conditions effective for said test agent to modulate the expression of the prostate cancer, and determining whether said test agent modulates said gene. An agent can modulate expression of a gene at any level, including transcription, translation, and/or perdurance of the nucleic acid (e.g., degradation, stability,  
30 etc.) in the cell. For modulating the biological activity of prostate cancer polypeptides, a method can comprise, in any effective order, one or more of the following steps, e.g., contacting a polypeptide (e.g., in a cell, lysate, or isolated) with a test agent under conditions



effective for said test agent to modulate the biological activity of said polypeptide, and determining whether said test agent modulates said biological activity.

Contacting a gene or polypeptide with the test agent can be accomplished by any suitable method and/or means that places the agent in a position to functionally control its expression or biological activity. Functional control indicates that the agent can exert its physiological effect on the gene or polypeptide through whatever mechanism it works. The choice of the method and/or means can depend upon the nature of the agent and the condition and type of environment in which the gene or polypeptide is presented, e.g., lysate, isolated, or in a cell population (such as, *in vivo*, *in vitro*, organ explants, etc.). For instance, if the cell population is an *in vitro* cell culture, the agent can be contacted with the cells by adding it directly into the culture medium. If the agent cannot dissolve readily in an aqueous medium, it can be incorporated into liposomes, or another lipophilic carrier, and then administered to the cell culture. Contact can also be facilitated by incorporation of agent with carriers and delivery molecules and complexes, by injection, by infusion, etc.

After the agent has been administered in such a way that it can gain access to the gene or polypeptide, it can be determined whether the test agent modulates the gene or polypeptide expression or biological activity. Modulation can be of any type, quality, or quantity, e.g., increase, facilitate, enhance, up-regulate, stimulate, activate, amplify, augment, induce, decrease, down-regulate, diminish, lessen, reduce, etc. The modulatory quantity can also encompass any value, e.g., 1%, 5%, 10%, 50%, 75%, 1-fold, 2-fold, 5-fold, 10-fold, 100-fold, etc. To modulate gene expression means, e.g., that the test agent has an effect on its expression, e.g., to effect the amount of transcription, to effect RNA splicing, to effect translation of the RNA into polypeptide, to effect RNA or polypeptide stability, to effect polyadenylation or other processing of the RNA, to effect post-transcriptional or post-translational processing, etc. To modulate biological activity means, e.g., that a functional activity of the polypeptide is changed in comparison to its normal activity in the absence of the agent. This effect includes, increase, decrease, block, inhibit, enhance, etc.

A test agent can be of any molecular composition, e.g., chemical compounds, biomolecules, such as polypeptides, lipids, nucleic acids (e.g., antisense to a polynucleotide sequence selected from Tables 1 and 2, or genomic sequences thereof), carbohydrates, antibodies, ribozymes, double-stranded RNA, aptamers, etc. For example, if a polypeptide to be modulated is a cell-surface molecule, a test agent can be an antibody that specifically recognizes it and, e.g., causes the polypeptide to be internalized, leading to its down

regulation on the surface of the cell. Such an effect does not have to be permanent, but can require the presence of the antibody to continue the down-regulatory effect. Antibodies can also be used to modulate the biological activity a polypeptide in a lysate or other cell-free form. Antisense can also be used as test agents to modulate gene expression.

5

#### Markers

The polynucleotides of the present invention can be used with other markers, especially prostate and prostate cancer markers to identity, detect, stage, diagnosis, determine, prognosticate, treat, etc., tissue, diseases and conditions, etc, of the prostate.

10 Markers can be polynucleotides, polypeptides, antibodies, ligands, specific binding partners, etc.

A number of genes and gene products have been identified which are associated with prostate cancer metastasis and/or progression, e.g., PSA, KAI1 (shows decreased expression in metastatic cells; Dong et al., *Science*, 268:884-6, 1995), D44 isoforms (differentially-regulated during carcinoma progression; Noordzij et al., *Clin. Cancer Res.*, 3:805-15, 1997), p53 (Effert et al., *J. Urol.*, 150:257-61, 1993), Rb, CDKN2, E-cadherin, PTEN (Hamilton et al., *Br. J. Cancer*, 82:1671-6, 2000; Dong et al., *Clin. Cancer Res.*, 7:304-308, 2001), bcl-2, prostatic acid phosphatase (PAP), prostate specific membrane antigen (e.g., U.S. Pat. Nos. 5,538,866 and 6,107,090), Smad3 (e.g., Kang et al., *Proc. Natl. Acad. Sci.*, 98:3018-3023, 2001), TGF-beta, and other oncogenes and tumor suppressor genes. See, also, Myers and Grizzle, *Eur. Urol.*, 30:153-166, 1996, for other biomarkers associated with prostatic carcinoma, such as PCNA, p185-erbB-2, p180erbB-3, TAG-72, nm23-H1 and FASE. Such markers can be used in combination with the methods of the present invention to facilitate identifying, grading, staging, prognostication, etc, of conditions and diseases of the prostate.

25

#### Therapeutics

Selective polynucleotides, polypeptides, and specific-binding partners thereto, can be utilized in therapeutic applications, especially to treat prostate cancer. Useful methods include, but are not limited to, immunotherapy (e.g., using specific-binding partners to polypeptides), vaccination (e.g., using a selective polypeptide or a naked DNA encoding such polypeptide), protein or polypeptide replacement therapy, gene therapy (e.g., germ-line correction, antisense), etc.

30 Various immunotherapeutic approaches can be used. For instance, unlabeled

antibody that specifically recognizes a tissue-specific antigen can be used to stimulate the body to destroy or attack the cancer, to cause down-regulation, to produce complement-mediated lysis, to inhibit cell growth, etc., of target cells which display the antigen, e.g., analogously to how c-erbB-2 antibodies are used to treat breast cancer. In addition, antibody  
5 can be labeled or conjugated to enhance its deleterious effect, e.g., with radionuclides and other energy emitting entities, toxins, such as ricin, exotoxin A (ETA), and diphtheria, cytotoxic or cytostatic agents, immunomodulators, chemotherapeutic agents, etc. See, e.g., U.S. Pat. No. 6,107,090.

An antibody or other specific-binding partner can be conjugated to a second molecule,  
10 such as a cytotoxic agent, and used for targeting the second molecule to a tissue-antigen positive cell (Vitetta, E. S. et al., 1993, Immunotoxin therapy, in DeVita, Jr., V. T. et al., eds, Cancer: Principles and Practice of Oncology, 4th ed., J. B. Lippincott Co., Philadelphia, 2624-2636). Examples of cytotoxic agents include, but are not limited to, antimetabolites, alkylating agents, anthracyclines, antibiotics, anti-mitotic agents, radioisotopes and  
15 chemotherapeutic agents. Further examples of cytotoxic agents include, but are not limited to ricin, doxorubicin, daunorubicin, taxol, ethidium bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, 1-dehydrotestosterone, diphtheria toxin, Pseudomonas exotoxin (PE) A, PE40, abrin, elongation factor-2 and glucocorticoid. Techniques for conjugating therapeutic agents to antibodies are  
20 well.

In addition to immunotherapy, polynucleotides and polypeptides can be used as targets for non-immunotherapeutic applications, e.g., using compounds which interfere with function, expression (e.g., antisense as a therapeutic agent), assembly, etc. RNA interference can be used in vitro and in vivo to silence differentially-expressed genes when its  
25 expression contributes to a disease (but also for other purposes, e.g., to identify the gene's function to change a developmental pathway of a cell, etc.). See, e.g., Sharp and Zamore, *Science*, 287:2431-2433, 2001; Grishok et al., *Science*, 287:2494, 2001.

Delivery of therapeutic agents can be achieved according to any effective method, including, liposomes, viruses, plasmid vectors, bacterial delivery systems, orally,  
30 systemically, etc. Therapeutic agents of the present invention can be administered in any form by any effective route, including, e.g., oral, parenteral, enteral, intraperitoneal, topical, transdermal (e.g., using any standard patch), ophthalmic, nasally, local, non-oral, such as aerosol, inhalation, subcutaneous, intramuscular, buccal, sublingual, rectal, vaginal, intra-

arterial, and intrathecal, etc. They can be administered alone, or in combination with any ingredient(s), active or inactive.

In addition to therapeutics, *per se*, the present invention also relates to methods of treating prostate cancer showing altered expression of differentially-regulated genes, such as Tables 1 and 2, comprising, e.g., administering to a subject in need thereof a therapeutic agent which is effective for regulating expression of said genes and/or which is effective in treating said disease. The term "treating" is used conventionally, e.g., the management or care of a subject for the purpose of combating, alleviating, reducing, relieving, improving the condition of, etc., of a disease or disorder. By the phrase "altered expression," it is meant that the disease is associated with a mutation in the gene, or any modification to the gene (or corresponding product) which affects its normal function. Thus, expression of a differentially-regulated gene refers to, e.g., transcription, translation, splicing, stability of the mRNA or protein product, activity of the gene product, differential expression, etc.

Any agent which "treats" the disease can be used. Such an agent can be one which regulates the expression of the gene. Expression refers to the same acts already mentioned, e.g. transcription, translation, splicing, stability of the mRNA or protein product, activity of the gene product, differential expression, etc. For instance, if the condition was a result of a complete deficiency of the gene product, administration of gene product to a patient would be said to treat the disease and regulate the gene's expression. Many other possible situations are possible, e.g., where the gene is aberrantly expressed, and the therapeutic agent regulates the aberrant expression by restoring its normal expression pattern.

## Antisense

Antisense polynucleotide (e.g., RNA) can also be prepared from a polynucleotide according to the present invention, preferably an anti-sense to a gene of Tables 1 and 2. Antisense polynucleotide can be used in various ways, such as to regulate or modulate expression of the polypeptides they encode, e.g., inhibit their expression, for in situ hybridization, for therapeutic purposes, for making targeted mutations (in vivo, triplex, etc.) etc. For guidance on administering and designing anti-sense, see, e.g., U.S. Pat. Nos. 6,200,960, 6,200,807, 6,197,584, 6,190,869, 6,190,661, 6,187,587, 6,168,950, 6,153,595, 6,150,162, 6,133,246, 6,117,847, 6,096,722, 6,087,343, 6,040,296, 6,005,095, 5,998,383,

5,994,230, 5,891,725, 5,885,970, and 5,840,708. An antisense polynucleotides can be operably linked to an expression control sequence. A total length of about 35 bp can be used in cell culture with cationic liposomes to facilitate cellular uptake, but for *in vivo* use, preferably shorter oligonucleotides are administered, e.g. 25 nucleotides.

5       Antisense polynucleotides can comprise modified, nonnaturally-occurring nucleotides and linkages between the nucleotides (e.g., modification of the phosphate-sugar backbone; methyl phosphonate, phosphorothioate, or phosphorodithioate linkages; and 2'-O-methyl ribose sugar units), e.g., to enhance *in vivo* or *in vitro* stability, to confer nuclease resistance, to modulate uptake, to modulate cellular distribution and compartmentalization, etc. Any  
10       effective nucleotide or modification can be used, including those already mentioned, as known in the art, etc., e.g., disclosed in U.S. Pat. Nos. 6,133,438; 6,127,533; 6,124,445; 6,121,437; 5,218,103 (e.g., nucleoside thiophosphoramidites); 4,973,679; Sproat et al., "2'-O-Methyloligoribonucleotides: synthesis and applications," *Oligonucleotides and Analogs A Practical Approach*, Eckstein (ed.), IRL Press, Oxford, 1991, 49-86; Iribarren et al., "2'-O-  
15       Alkyl Oligoribonucleotides as Antisense Probes," *Proc. Natl. Acad. Sci. USA*, 1990, 87, 7747-7751; Cotton et al., "2'-O-methyl, 2'-O-ethyl oligoribonucleotides and phosphorothioate oligodeoxyribonucleotides as inhibitors of the *in vitro* U7 snRNP-dependent mRNA processing event," *Nucl. Acids Res.*, 1991, 19, 2629-2635.

## 20       Arrays

      The present invention also relates to an ordered array of polynucleotide probes and specific-binding partners (e.g., antibodies) for detecting the expression of differentially-regulated genes in a sample, comprising, one or more polynucleotide probes or specific  
25       binding partners associated with a solid support, wherein each probe is specific for said genes, and the probes comprise a nucleotide sequence of Tables 1 and 2 which is specific for said gene, a nucleotide sequence having sequence identity to Tables 1 and 2 which is specific for said gene or polynucleotide, or complements thereto, or a specific-binding partner which is specific for said genes.

      The phrase "ordered array" indicates that the probes are arranged in an identifiable or  
30       position-addressable pattern, e.g., such as the arrays disclosed in U.S. Pat. Nos. 6,156,501, 6,077,673, 6,054,270, 5,723,320, 5,700,637, WO09919711, WO00023803. The probes are associated with the solid support in any effective way. For instance, the probes can be bound to the solid support, either by polymerizing the probes on the substrate, or by attaching a

probe to the substrate. Association can be, covalent, electrostatic, noncovalent, hydrophobic, hydrophilic, noncovalent, coordination, adsorbed, absorbed, polar, etc. When fibers or hollow filaments are utilized for the array, the probes can fill the hollow orifice, be absorbed into the solid filament, be attached to the surface of the orifice, etc. Probes can be of any effective size, sequence identity, composition, etc., as already discussed.

Ordered arrays can further comprise polynucleotide probes or specific-binding partners which are specific for other genes, including genes specific for prostate or disorders associated with prostate, such as prostate cancer.

#### 10 Transgenic animals

The present invention also relates to transgenic animals comprising differentially-regulated genes of the present invention. Such genes, as discussed in more detail below, include, but are not limited to, functionally-disrupted genes, mutated genes, ectopically or selectively-expressed genes, inducible or regulatable genes, etc. These transgenic animals can be produced according to any suitable technique or method, including homologous recombination, mutagenesis (e.g., ENU, Rathkolb et al., *Exp. Physiol.*, 85(6):635-644, 2000), and the tetracycline-regulated gene expression system (e.g., U.S. Pat. No. 6,242,667). The term "gene" as used herein includes any part of a gene, i.e., regulatory sequences, promoters, enhancers, exons, introns, coding sequences, etc. The nucleic acid present in the construct or transgene can be naturally-occurring wild-type, polymorphic, or mutated.

Along these lines, polynucleotides of the present invention can be used to create transgenic animals, e.g. a non-human animal, comprising at least one cell whose genome comprises a functional disruption of a differentially-regulated gene. By the phrases "functional disruption" or "functionally disrupted," it is meant that the gene does not express a biologically-active product. It can be substantially deficient in at least one functional activity coded for by the gene. Expression of a polypeptide can be substantially absent, i.e., essentially undetectable amounts are made. However, polypeptide can also be made, but which is deficient in activity, e.g., where only an amino-terminal portion of the gene product is produced.

The transgenic animal can comprise one or more cells. When substantially all its cells contain the engineered gene, it can be referred to as a transgenic animal "whose genome comprises" the engineered gene. This indicates that the endogenous gene loci of the animal has been modified and substantially all cells contain such modification.

Functional disruption of the gene can be accomplished in any effective way, including, e.g., introduction of a stop codon into any part of the coding sequence such that the resulting polypeptide is biologically inactive (e.g., because it lacks a catalytic domain, a ligand binding domain, etc.), introduction of a mutation into a promoter or other regulatory sequence that is effective to turn it off, or reduce transcription of the gene, insertion of an exogenous sequence into the gene which inactivates it (e.g., which disrupts the production of a biologically-active polypeptide or which disrupts the promoter or other transcriptional machinery), deletion of sequences from the a differentially-regulated gene, etc. Examples of transgenic animals having functionally disrupted genes are well known, e.g., as described in U.S. Pat. Nos. 6,239,326, 6,225,525, 6,207,878, 6,194,633, 6,187,992, 6,180,849, 6,177,610, 6,100,445, 6,087,555, 6,080,910, 6,069,297, 6,060,642, 6,028,244, 6,013,858, 5,981,830, 5,866,760, 5,859,314, 5,850,004, 5,817,912, 5,789,654, 5,777,195, and 5,569,824. A transgenic animal which comprises the functional disruption can also be referred to as a "knock-out" animal, since the biological activity of its a differentially-regulated gene has been "knocked-out." Knock-outs can be homozygous or heterozygous.

For creating functional disrupted genes, and other gene mutations, homologous recombination technology is of special interest since it allows specific regions of the genome to be targeted. Using homologous recombination methods, genes can be specifically-inactivated, specific mutations can be introduced, and exogenous sequences can be introduced at specific sites. These methods are well known in the art, e.g., as described in the patents above. See, also, Robertson, *Biol. Reproduc.*, 44(2):238-245, 1991. Generally, the genetic engineering is performed in an embryonic stem (ES) cell, or other pluripotent cell line (e.g., adult stem cells, EG cells), and that genetically-modified cell (or nucleus) is used to create a whole organism. Nuclear transfer can be used in combination with homologous recombination technologies.

For example, a differentially-regulated gene locus can be disrupted in mouse ES cells using a positive-negative selection method (e.g., Mansour et al., *Nature*, 336:348-352, 1988). In this method, a targeting vector can be constructed which comprises a part of the gene to be targeted. A selectable marker, such as neomycin resistance genes, can be inserted into a differentially-regulated gene exon present in the targeting vector, disrupting it. When the vector recombines with the ES cell genome, it disrupts the function of the gene. The presence in the cell of the vector can be determined by expression of neomycin resistance. See, e.g., U.S. Pat. No. 6,239,326. Cells having at least one functionally disrupted gene can

be used to make chimeric and germline animals, e.g., animals having somatic and/or germ cells comprising the engineered gene. Homozygous knock-out animals can be obtained from breeding heterozygous knock-out animals. See, e.g., U.S. Pat. No. 6,225,525.

A transgenic animal, or animal cell, lacking one or more functional differentially-regulated genes can be useful in a variety of applications, including, as an animal model for cancer, for drug screening assays, as a source of tissues deficient in said gene activity, and any of the utilities mentioned in any issued U.S. Patent on transgenic animals, including, U.S. Pat. Nos. 6,239,326, 6,225,525, 6,207,878, 6,194,633, 6,187,992, 6,180,849, 6,177,610, 6,100,445, 6,087,555, 6,080,910, 6,069,297, 6,060,642, 6,028,244, 6,013,858, 5,981,830, 5,866,760, 5,859,314, 5,850,004, 5,817,912, 5,789,654, 5,777,195, and 5,569,824.

The present invention also relates to non-human, transgenic animal whose genome comprises recombinant a differentially-regulated gene nucleic acid operatively linked to an expression control sequence effective to express said coding sequence, e.g., in prostate. such a transgenic animal can also be referred to as a “knock-in” animal since an exogenous gene has been introduced, stably, into its genome.

A recombinant a differentially-regulated gene nucleic acid refers to a gene which has been introduced into a target host cell and optionally modified, such as cells derived from animals, plants, bacteria, yeast, etc. A recombinant a differentially-regulated gene includes completely synthetic nucleic acid sequences, semi-synthetic nucleic acid sequences, sequences derived from natural sources, and chimeras thereof. “Operable linkage” has the meaning used through the specification, i.e., placed in a functional relationship with another nucleic acid. When a gene is operably linked to an expression control sequence, as explained above, it indicates that the gene (e.g., coding sequence) is joined to the expression control sequence (e.g., promoter) in such a way that facilitates transcription and translation of the coding sequence. As described above, the phrase “genome” indicates that the genome of the cell has been modified. In this case, the recombinant a differentially-regulated gene has been stably integrated into the genome of the animal. The a differentially-regulated gene nucleic acid in operable linkage with the expression control sequence can also be referred to as a construct or transgene.

Any expression control sequence can be used depending on the purpose. For instance, if selective expression is desired, then expression control sequences which limit its expression can be selected. These include, e.g., tissue or cell-specific promoters, introns, enhancers, etc. For various methods of cell and tissue-specific expression, see, e.g., U.S. Pat.



Nos. 6,215,040, 6,210,736, and 6,153,427. These also include the endogenous promoter, i.e., the coding sequence can be operably linked to its own promoter. Inducible and regulatable promoters can also be utilized.

The present invention also relates to a transgenic animal which contains a functionally  
5 disrupted and a transgene stably integrated into the animals genome. Such an animal can be constructed using combinations any of the above- and below-mentioned methods. Such animals have any of the aforementioned uses, including permitting the knock-out of the normal gene and its replacement with a mutated gene. Such a transgene can be integrated at the endogenous gene locus so that the functional disruption and "knock-in" are carried out in  
10 the same step.

In addition to the methods mentioned above, transgenic animals can be prepared according to known methods, including, e.g., by pronuclear injection of recombinant genes into pronuclei of 1-cell embryos, incorporating an artificial yeast chromosome into embryonic stem cells, gene targeting methods, embryonic stem cell methodology, cloning  
15 methods, nuclear transfer methods. See, also, e.g., U.S. Patent Nos. 4,736,866; 4,873,191; 4,873,316; 5,082,779; 5,304,489; 5,174,986; 5,175,384; 5,175,385; 5,221,778; Gordon et al., Proc. Natl. Acad. Sci., 77:7380-7384, 1980; Palmiter et al., Cell, 41:343-345, 1985; Palmiter et al., Ann. Rev. Genet., 20:465-499, 1986; Askew et al., Mol. Cell. Bio., 13:4115-4124, 1993; Games et al. Nature, 373:523-527, 1995; Valancius and Smithies, Mol. Cell. Bio.,  
20 11:1402-1408, 1991; Stacey et al., Mol. Cell. Bio., 14:1009-1016, 1994; Hasty et al., Nature, 350:243-246, 1995; Rubinstein et al., Nucl. Acid Res., 21:2613-2617, 1993; Cibelli et al., Science, 280:1256-1258, 1998. For guidance on recombinase excision systems, see, e.g., U.S. Pat. Nos. 5,626,159, 5,527,695, and 5,434,066. See also, Orban, P.C., et al., "Tissue- and Site-Specific DNA Recombination in Transgenic Mice," Proc. Natl. Acad. Sci. USA,  
25 89:6861-6865 (1992); O'Gorman, S., et al., "Recombinase-Mediated Gene Activation and Site-Specific Integration in Mammalian Cells," Science, 251:1351-1355 (1991); Sauer, B., et al., "Cre-stimulated recombination at loxP-Containing DNA sequences placed into the mammalian genome," Polynucleotides Research, 17(1):147-161 (1989); Gagneten, S. et al. (1997) Nucl. Acids Res. 25:3326-3331; Xiao and Weaver (1997) Nucl. Acids Res. 25:2985-  
30 2991; Agah, R. et al. (1997) J. Clin. Invest. 100:169-179; Barlow, C. et al. (1997) Nucl. Acids Res. 25:2543-2545; Araki, K. et al. (1997) Nucl. Acids Res. 25:868-872; Mortensen, R. N. et al. (1992) Mol. Cell. Biol. 12:2391-2395 (G418 escalation method); Lakhiani, P. P. et al. (1997) Proc. Natl. Acad. Sci. USA 94:9950-9955 ("hit and run"); Westphal and Leder

(1997) Curr. Biol. 7:530-533 (transposon-generated “knock-out” and “knock-in”); Templeton, N. S. et al. (1997) Gene Ther. 4:700-709 (methods for efficient gene targeting, allowing for a high frequency of homologous recombination events, e.g., without selectable markers); PCT International Publication WO 93/22443 (functionally-disrupted).

5           A polynucleotide according to the present invention can be introduced into any non-human animal, including a non-human mammal, mouse (Hogan et al., Manipulating the Mouse Embryo: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1986), pig (Hammer et al., Nature, 315:343-345, 1985), sheep (Hammer et al., Nature, 315:343-345, 1985), cattle, rat, or primate. See also, e.g., Church, 1987, Trends in  
10 Biotech. 5:13-19; Clark et al., Trends in Biotech. 5:20-24, 1987); and DePamphilis et al., BioTechniques, 6:662-680, 1988. Transgenic animals can be produced by the methods described in U.S. Pat. No. 5,994,618, and utilized for any of the utilities described therein.

#### Database

15           The present invention also relates to electronic forms of polynucleotides, polypeptides, etc., of the present invention, including computer-readable medium (e.g., magnetic, optical, etc., stored in any suitable format, such as flat files or hierarchical files) which comprise such sequences, or fragments thereof, e-commerce-related means, etc. Along these lines, the present invention relates to methods of retrieving gene sequences from  
20 a computer-readable medium, comprising, one or more of the following steps in any effective order, e.g., selecting a cell or gene expression profile, e.g., a profile that specifies that said gene is differentially expressed in prostate cancer, and retrieving said differentially expressed gene sequences, where the gene sequences consist of the genes represented by Tables 1 and 2.

25           A “gene expression profile” means the list of tissues, cells, etc., in which a defined gene is expressed (i.e, transcribed and/or translated). A “cell expression profile” means the genes which are expressed in the particular cell type. The profile can be a list of the tissues in which the gene is expressed, but can include additional information as well, including level of expression (e.g., a quantity as compared or normalized to a control gene), and  
30 information on temporal (e.g., at what point in the cell-cycle or developmental program) and spatial expression. By the phrase “selecting a gene or cell expression profile,” it is meant that a user decides what type of gene or cell expression pattern he is interested in retrieving, e.g., he may require that the gene is differentially expressed in a tissue, or he may require that the

gene is not expressed in blood, but must be expressed in prostate cancer. Any pattern of expression preferences may be selected. The selecting can be performed by any effective method. In general, "selecting" refers to the process in which a user forms a query that is used to search a database of gene expression profiles. The step of retrieving involves  
5 searching for results in a database that correspond to the query set forth in the selecting step. Any suitable algorithm can be utilized to perform the search query, including algorithms that look for matches, or that perform optimization between query and data. The database is information that has been stored in an appropriate storage medium, having a suitable computer-readable format. Once results are retrieved, they can be displayed in any suitable  
10 format, such as HTML.

For instance, the user may be interested in identifying genes that are differentially expressed in a prostate cancer. He may not care whether small amounts of expression occur in other tissues, as long as such genes are not expressed in peripheral blood lymphocytes. A query is formed by the user to retrieve the set of genes from the database having the desired  
15 gene or cell expression profile. Once the query is inputted into the system, a search algorithm is used to interrogate the database, and retrieve results.

#### Advertising, licensing, etc., methods

The present invention also relates to methods of advertising, licensing, selling,  
20 purchasing, brokering, etc., genes, polynucleotides, specific-binding partners, antibodies, etc., of the present invention. Methods can comprises, e.g., displaying a a differentially-regulated gene gene, a differentially-regulated gene polypeptide, or antibody specific for a differentially-regulated gene in a printed or computer-readable medium (e.g., on the Web or Internet), accepting an offer to purchase said gene, polypeptide, or antibody.

25

#### Other

A polynucleotide, probe, polypeptide, antibody, specific-binding partner, etc., according to the present invention can be isolated. The term "isolated" means that the material is in a form in which it is not found in its original environment or in nature, e.g.,  
30 more concentrated, more purified, separated from component, etc. An isolated polynucleotide includes, e.g., a polynucleotide having the sequenced separated from the chromosomal DNA found in a living animal, e.g., as the complete gene, a transcript, or a cDNA. This polynucleotide can be part of a vector or inserted into a chromosome (by

specific gene-targeting or by random integration at a position other than its normal position) and still be isolated in that it is not in a form that is found in its natural environment. A polynucleotide, polypeptide, etc., of the present invention can also be substantially purified. By substantially purified, it is meant that polynucleotide or polypeptide is separated and is  
5 essentially free from other polynucleotides or polypeptides, i.e., the polynucleotide or polypeptide is the primary and active constituent. A polynucleotide can also be a recombinant molecule. By "recombinant," it is meant that the polynucleotide is an arrangement or form which does not occur in nature. For instance, a recombinant molecule comprising a promoter sequence would not encompass the naturally-occurring  
10 gene, but would include the promoter operably linked to a coding sequence not associated with it in nature, e.g., a reporter gene, or a truncation of the normal coding sequence.

The term "marker" is used herein to indicate a means for detecting or labeling a target. A marker can be a polynucleotide (usually referred to as a "probe"), polypeptide (e.g., an antibody conjugated to a detectable label), PNA, or any effective material.

15 The topic headings set forth above are meant as guidance where certain information can be found in the application, but are not intended to be the only source in the application where information on such topic can be found.

#### Reference materials

20 For other aspects of the polynucleotides, reference is made to standard textbooks of molecular biology. See, e.g., Hames et al., Polynucleotide Hybridization, IL Press, 1985; Davis et al., Basic Methods in Molecular Biology, Elsevir Sciences Publishing, Inc., New York, 1986; Sambrook et al., Molecular Cloning, CSH Press, 1989; Howe, Gene Cloning and Manipulation, Cambridge University Press, 1995; Ausubel et al., Current Protocols in  
25 Molecular Biology, John Wiley & Sons, Inc., 1994-1998.

The preceding description, utilize the present invention to its fullest extent. The preceding preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limiting the remainder of the disclosure in any way whatsoever. The entire disclosure of all applications, patents and publications, cited above and in the figures  
30 are hereby incorporated by reference in their entirety.

## Claims:

1. A method for diagnosing a prostate cancer in a sample comprising prostate tissue, comprising:

5 determining the number of target genes which are differentially-regulated in said sample, wherein said target genes are selected from SEQ ID NO 1-211 of claim 26, whereby said number is indicative of the probability that said sample comprises prostate cancer.

2. A method of claim 1, wherein said determining is performed by Northern  
10 blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization using polynucleotide probes specific for genes selected from SEQ ID NO 1-211 of claim 26.

3. A method of claim 1, wherein said determining is performed by:  
15 contacting said sample with a polynucleotide probe under conditions effective for said probe to hybridize specifically to a target nucleic acid in said sample, and detecting the amount of hybridization between said probe and target nucleic acid, and  
comparing the amount of hybridization in said sample with the amount of  
20 hybridization of said probe in a second sample comprising normal prostate tissue.

4. A method of claim 1, wherein said determining is performed by:  
contacting said sample with a polynucleotide probe under conditions effective for  
said probe to hybridize specifically to a target nucleic acid in said sample, and  
25 detecting the amount of hybridization between said probe and target nucleic acid, and  
comparing the amount of hybridization in said sample with the amount of  
hybridization between a second probe and its corresponding second target nucleic acid in  
said sample.

30

5. A method of claim 2, wherein said probe is a contiguous sequence of at least 8 nucleotides selected from a polynucleotide sequence selected from SEQ ID NOS 1-107 of claim 26, or a complement thereto.

5 6. A method of assessing a therapeutic or preventative intervention in a subject having a prostate cancer, comprising,  
determining the expression levels in a sample comprising prostate tissue of target genes which are differentially-regulated in prostate cancer,  
wherein said target genes are selected from SEQ ID NO 1-211 of claim 26.

10 7. A method of claim 6, wherein the expression levels of at least 10 genes are determined.

8. A method of claim 6, wherein the determining is performed by Northern blot  
15 analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization using polynucleotide probes specific for genes selected from SEQ IDS NO 1-211 of claim 26.

9. A method for identifying agents that modulate the expression of target  
20 polynucleotides differentially-regulated in prostate cancer cells, comprising,  
contacting a prostate cell population with a test agent under conditions effective for said test agent to modulate the expression of a target polynucleotide in said cell population,  
and  
determining whether said test agent modulates said target polynucleotide expression,  
25 wherein said target polynucleotide is selected from SEQ ID NOS 1-107 of claim 26.

10. A method of claim 9, wherein said agent is an antisense polynucleotide to said target polynucleotide sequence and which is effective to inhibit translation of said target polynucleotide.

11. A method for identifying agents that modulate a biological activity of a polypeptide differentially-regulated in prostate cancer cells, comprising,

contacting a polypeptide differentially-regulated in prostate cancer cells with a test agent under conditions effective for said test agent to modulate a biological activity of said polypeptide, and

determining whether said test agent modulates said biological activity, wherein said polypeptide is selected from SEQ ID NOS 108-211 of claim 26.

12. A method of treating prostate cancer, comprising,

administering to a subject in need thereof a therapeutic agent which is effective for regulating expression of at least one sequence selected from SEQ ID NOS 1-211 of claim 26.

13. A method of claim 12, wherein said agent is an antibody or an antisense

which is effective to inhibit translation of said gene.

14. A method of diagnosing a prostate cancer comprising:

assessing the expression of at least one gene selected from SEQ ID NO 1-211 of claim 26, wherein said gene is differentially-regulated in said cancer.

15. A method of claim 14, wherein assessing is:

measuring mRNA expression levels of said or measuring the expression levels of polypeptide coded for by said gene.

16. A method of claim 14, further comprising:

comparing said expression to the expression of said polynucleotide in a known normal tissue.

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17. A method of claim 14, wherein said assessing detecting is performed by:  
Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR,  
RACE PCR, or *in situ* hybridization, and  
using a polynucleotide probe specific for a polynucleotide sequence selected from  
5 SEQ ID NOS 1-107 of claim 26.

18. A method of claim 14, wherein the expression of at least one up-regulated  
polynucleotide and at least one down-regulated polynucleotide are assessed.

10 19. A method of claim 14, wherein the expression of at least five up-regulated  
polynucleotides and at least five down-regulated polynucleotides are assessed.

20. A method of retrieving prostate cancer differentially-regulated gene  
sequences from a computer-readable medium, comprising:

15 selecting a gene expression profile that specifies that said gene is differentially-  
regulated in a prostate cancer, and retrieving prostate cancer differentially-regulated gene  
sequences,  
where the gene sequences consist of genes selected from SEQ ID NO 1-211 of claim  
26.

20

21. An ordered array of polynucleotide probes for detecting the expression of  
differentially-regulated prostate cancer genes in a sample, comprising:  
polynucleotide probes associated with a solid support, wherein each probe is specific  
for a different differentially-regulated prostate cancer gene, and the probes are specific for  
25 genes selected from SEQ ID NO 1-211 of claim 26.

22. An array of claim 21, wherein said array comprises probes specific for up-  
regulated and down-regulated polynucleotides.

30

23. A method of advertising for sale, commercial use, or licensing, comprising:  
displaying at least one polynucleotide or polypeptide sequence selected from



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SEQ ID NO 1-211 of claim 26, or a complement thereto.

24. A non-human, transgenic mammal having a functional disruption in at least one gene selected from SEQ ID NO 1-211 of claim 26, and which is susceptible to prostate  
5 cancer.

25. A cell expression profile consisting of the expression pattern of a prostate cancer tissue sample for differentially-regulated genes of claim 26.

10 26. A plurality of genes which are differentially regulated in a prostate cancer, selected from:  
up-regulated genes having SEQ ID NOS 1-75 and 140-211; and  
down-regulated genes having SEQ ID 76-107 and 108-139.

15

Table 1

DNA SEQ ID	Prt SEQ ID	Identifier	Exp	GI#	Gene Name and Description
1	140	PC030931U	U	337504	HUMRPS24A Human ribosomal protein S24 mRNA
2	141	PC010049U	U	3978243	AF070674 Homo sapiens inhibitor of apoptosis protein-1 (MIHC) mRNA complete cds
3	142	PC010039U	U	6912451	NM_012289.1 Homo sapiens Ketch-like ECH-associated protein 1 (KIAA0132)
4	143	PC010957U	U	4557844	NM_001034.1 Homo sapiens ribonucleotide reductase M2 polypeptide (RRM2) mRNA
5	144	PC020728U	U	4503478	NM_001960.1 Homo sapiens eukaryotic translation elongation factor 1 delta
6	145	PC021342U	U	340057	HUMIUB Human poly-ubiquitin mRNA complete cds
7	146	PC030732U	U	4504374	Homo sapiens H factor 1 (complement) (HF1) mRNA
8		PC011348U	U	3093338	HSY17176 Homo sapiens mRNA for KIAA0976 protein complete cds
9	147	PC041029U	U	4589595	AB023193 Homo sapiens mRNA for KIAA0976 protein complete cds
10	148	PC040972U	U	4885132	Homo sapiens centromere protein F (400KD) (GENPF) mRNA
11	149	PC050853U	U	4503724	NM_000801.1 Homo sapiens FK506-binding protein 1A (12kD) (FKBP1A) mRNA
12	150	PC040158U	U	4826949	Homo sapiens kallikrein 7 (chymotryptic stratum corneum) (KLK7) mRNA
13	151	PC040441U	U	4826879	Homo sapiens oxidase (cytochrome c) assembly 1-like (OXA1L) mRNA
14	152	PC051210U	U	4506056	NM_002731.1 Homo sapiens protein kinase, cAMP-dependent, catalytic, beta
15	154	PC050296U	U	5453633	Homo sapiens dynein cytoplasmic light intermediate polypeptide 2 (DNCL12) mRNA
16	155	PC050151U	U	6715599	NM_002078.2 Homo sapiens golgi autoantigen, golgin subfamily a, 4
17	156	PC050149U	U	2217930	AB004884 Homo sapiens mRNA for PKU-alpha,
18	157	PC052095U	U	641957	HUMMYOHC Human nonmuscle myosin heavy chain-B (MYH10) mRNA partial cds
19	158	PC052029U	U	5803218	Homo sapiens serine protease inhibitor Kazal type 5 (SPINK5) mRNA
20	159	PC050620U	U	4504580	NM_003641.1 Homo sapiens interferon induced transmembrane protein 1, (IFITM1), mRNA
21	160	PC041338U	U	8051620	Homo sapiens 2'5'-oligoadenylate synthetase 1 (OAS1) transcript variant E18 mRNA
22	161	PC041980U	U	6735451	HSA271091 Homo sapiens mRNA for B-ind1 protein (B-ind1 gene)
23	162	PC060474U	U	4759321	Homo sapiens wingless-type MMTV integration site family member 2B (WNT2B) mRNA
24	163	PC060443U	U	4506730	Homo sapiens ribosomal protein S6 (RPS6) mRNA
25	164	PC060441U	U	1688257	HSU78045 Human collagenase and stromelysin genes, complete cds, and metalloelastase gene, partial cds
26	165	PC070152U	U	4506712	Homo sapiens ribosomal protein S27a (RPS27A) mRNA
27	166	PC060529U	U	4503820	Homo sapiens FYN-binding protein (FYN-120130) (FYN) mRNA and translated products
28	167	PC080348U	U	9623360	AF261688 Homo sapiens DNA polymerase epsilon p12 subunit gene, complete cds
29	168	PC070544U	U	1679960	S42658 S3 ribosomal protein [human colon mRNA 826 nt]
30	169	PC070343U	U	4507210	Homo sapiens signal recognition particle 14kD (homologous Alu RNA-binding protein) (SRP14) mRNA
31	170	PC061477U	U	4506386	Homo sapiens RAD23 (S. cerevisiae) homolog B (RAD23B) mRNA
32	171	PC060940U	U	5052074	Homo sapiens PAPS synthetase-2 (PAPSS2) mRNA
33	172	PC061779U	U	4504766	Homo sapiens integrin beta 1 (fibronectin receptor beta polypeptide antigen CD29 includes MDF2 MSK12) (ITGB1) mRNA
34	173	PC061839U	U	8394498	Homo sapiens ubiquitin associated protein (UBAP) mRNA
35	174	PC061827U	U	7382495	Homo sapiens ubiquitin associated protein (UBAP) mRNA
36	175	PC080511U	U	4504190	NM_000179.1 Homo sapiens muS (E. coli) homolog 6 (MSH6)
37	176	PC090754U	U	4503472	Homo sapiens eukaryotic translation elongation factor 1 (yeast Ste20-related) (PAK1) mRNA
38	177	PC090842U	U	4557031	Homo sapiens eukaryotic translation elongation factor 1 alpha 1-like 14 (EEF1A1L14) mRNA
39	178	PC091028U	U	7662425	Homo sapiens lactate dehydrogenase B (LDHB) mRNA
40		PC070890U	U	6531675	AF205588.1AF205588 Homo sapiens ZNF01 and HUMORFKG1B genes
41		PC071851U	U	3090894	AF052497 Homo sapiens clone B18 unknown mRNA
42	179	PC070729U	U	8923790	Homo sapiens r15 beta protein (HSRTSBETA) mRNA

Table 1

43	180	PC080742U	U	4507186	NM_003125.1	Homo sapiens small proline-rich protein 1B (cornifin)
44	181	PC100113U	U	6647292	AF166330.2	Homo sapiens stratum corneum chymotryptic enzyme gene
45		PC100356U	U	3093334	HSY17172	Homo sapiens mRNA from HIV-associated non-Hodgkin's lymphoma (clone h12-22)
46	182	PC100428U	U	4502980	NM_001861.1	Homo sapiens cytochrome c oxidase subunit IV (COX4)
47	183	PC090230U	U	3252910	AF056322	Homo sapiens SP100-HMG nuclear autoantigen (SP100) mRNA complete cds
48	184	PC090233U	U	4504192		Homo sapiens general transcription factor IIB (GTF2B) mRNA
49	185	PC101063U	U	35037	HSNFIV	H sapiens mRNA for nuclear factor IV
50	186	PC090825U	U	7706215		Homo sapiens H-2K binding factor-2 (LOC51580) mRNA
51	187	PC101430U	U	609453	M69199.1	HUMGOS2A Human GOS2 protein gene, complete cds
52	188	PC091425U	U	4732025	AF118569	Homo sapiens angiotensin I converting enzyme precursor
53	189	PC101434U	U	4505374	NM_002499.1	Homo sapiens neogenin (chicken) homolog 1
54	190	PC101039U	U	7657203		Homo sapiens acidic 82 kDa protein mRNA (HSU15552) mRNA
55	191	PC101037U	U	6005813		Homo sapiens serine threonine protein kinase (NDR) mRNA
56	192	PC101033U	U	7662579		Homo sapiens PRO0644 protein (PRO0644) mRNA
57	193	PC020165U	U	7669502	NM_013995.1	Homo sapiens lysosomal-associated membrane protein 2
58	194	PC020162U	U	4507164	NM_003113.1	Homo sapiens nuclear antigen Sp100 (SP100) mRNA
59	195	PC030247U	U	348706	HUMCATHBS	Homo sapiens cathepsin B mRNA 3' UTR with a stem-loop structure providing mRNA stability
60	196	PC030471U	U	31396	HSFIB1	Human mRNA for fibronectin (FN precursor)
61	197	PC030454U	U	4506678		Homo sapiens ribosomal protein S10 (RPS10) mRNA
62	198	PC030326U	U	4507148		Homo sapiens superoxide dismutase 1 soluble (amyotrophic lateral sclerosis 1 (adult)) (SOD1) mRNA
63	199	PC030425U	U	415818	HSMK167	H.sapiens mki67a mRNA (long type) for antigen of monoclonal antibody Ki-67
64	200	PC091527U	U	5803091		Homo sapiens methionine aminopeptidase, aIF-2-associated p67 (MNPEP) mRNA
65	201	PC092004U	U	8922823	NM_018300.1	Homo sapiens hypothetical protein FLJ11015 (FLJ11015)
66	202	PC091888U	U	4757809		Homo sap/ ATP synthase H+ transporting mito.F1 complex alpha subunit isoform 1 cardiac muscle (ATP5A1) nuclear gene
67	203	PC091853U	U	31091	X16869.1	HSEF1AC Human mRNA for elongation factor 1-alpha
68	204	PC092052U	U	4505634		Homo sapiens BH-protocadherin (brain-heart) (9999DH7) mRNA
69	205	PC091839U	U	7186646	AF222043	Homo sapiens ubiquitin-associated protein (NAG20) mRNA complete cds
70	206	PC111181U	U	7416940	AF139077	Homo sapiens M5-14 mRNA complete cds
71	207	PC111168U	U	4759283	NM_004181.1	Homo sapiens ubiquitin carboxyl-terminal esterase L1
72	208	PC120136U	U	7706728		Homo sapiens TBX3-iso protein (TBX3-iso) mRNA
73	209	PC120331U	U	4504424	NM_002128.1	Homo sapiens high-mobility group (nonhistone chromosomal) protein 1
74	210	PC121671U	U	7661635		Homo sapiens DKFZP564O2082 protein (DKFZP564O2082) mRNA
75	211	PC020741U	U	7657624	NM_014393.1	Homo sapiens slaufen (Drosophila, RNA-binding protein) homolog 2
	153	PC051231U	U	4506600		Homo sapiens ribosomal protein L14 (RPL14) mRNA
		PC020627U	U	8923949		Homo sapiens ovarian cancer related protein OVN9-3 (OVN9-3) mRNA
		PC110927U	U	8923282	NM_017754.1	Homo sapiens hypothetical protein FLJ20302 (FLJ20302)

Table 2

DNA SEQ ID	Prt SEQ ID	Identifier	Exp	GI#	Gene Name and Description
76	108	PC040734D	D	5174656	NM_006096.1 Homo sapiens differentiation-related gene 1 nickel-specific induction protein
77	109	PC040156D	D	4505748	Homo sapiens phosphofructokinase muscle (PFKM) mRNA
78	110	PC051745D	D	4758751	Homo sapiens neuronal apoptosis inhibitory protein (NAIP) mRNA
79	111	PC042021D	D	4505986	Homo sapiens PTPRF interacting protein binding protein 1 (liprin beta 1) (PPFIBP1) mRNA and translated products
80	112	PC060144D	D	4758199	NM_004415.1 Homo sapiens desmoplakin (DPI, DPT1) (DSP) mRNA
81	113	PC080139D	D	7657159	NM_014362.1 Homo sapiens 3-hydroxyisobutyryl-Coenzyme A hydrolase (HIBCH) mRNA
82	114	PC080435D	D	4758807	Homo sapiens ras GTPase activating protein-like (NGAP) mRNA
83	115	PC070436D	D	9790904	NM_001924.1 Homo sapiens growth arrest and DNA-damage-inducible
84	116	PC061342D	D	186485	HUMINT04 Human leukocyte adhesion protein p15095 alpha subunit gene exons 16 - 21
85	117	PC060793D	D	4507582	NM_000043.1 Homo sapiens tumor necrosis factor receptor superfamily
86	118	PC060743D	D	4557256	Homo sapiens adenylate cyclase 8 (brain) (ADCY8) mRNA
87	119	PC061528D	D	4506700	Homo sapiens ribosomal protein S23 (RPS23) mRNA
88	120	PC090788D	D	5031638	Homo sapiens cornichon-like (CNIL) mRNA
89	121	PC090722D	D	7670747	AF227906 Homo sapiens UDP-glucosyltransferase 2 precursor mRNA complete cds
90	122	PC071770D	D	31441	HSPNRB Human mRNA for integrin beta 1 subunit
91	123	PC090677D	D	187701	HUMHBA123 Human MHC protein homologous to chicken B complex protein mRNA complete cds
92	124	PC101847D	D	5902021	Homo sapiens PL6 protein (PL6) mRNA
93	125	PC090622D	D	4506858	NM_002997.1 Homo sapiens syndecan 1 (SDC1) mRNA
94	126	PC010433D	D	4827043	Homo sapiens thyroid hormone receptor-associated protein 240 kDa subunit (TRAP240) mRNA
95	127	PC020238D	D	4503090	NM_001893.1 Homo sapiens casein kinase I, delta (CSNK1D) mRNA
96	128	PC030301D	D	4506728	Homo sapiens ribosomal protein S5 (RPS5) mRNA
97	129	PC110249D	D	4759257	Homo sapiens Ac-like transposable element (ALTE) mRNA
98	130	PC110341D	D	5031778	Homo sapiens interferon gamma-inducible protein 16 (IFI16) mRNA
99		PC110431D	D	3885367	AB019564 Homo sapiens mRNA expressed only in placental villi clone SMAP47
100	131	PC110940D	D	4758949	NM_000942.1 Homo sapiens penicillin-binding protein 1 (PBP1) mRNA
101	132	PC111588D	D	4503412	Homo sapiens diphtheria toxin receptor (heparin-binding epidermal growth factor-like growth factor) (DTR) mRNA
102	133	PC111669D	D	7705822	Homo sapiens N-terminal acetyltransferase complex and subunit (LOC511126) mRNA
103	134	PC032046D	D	7657325	NM_014623.1 Homo sapiens male-enhanced antigen (MEA)
104	135	PC120741D	D	5174388	NM_005891.1 Homo sapiens acetyl-Coenzyme A acetyltransferase 2
105	136	PC120740D	D	311380	HSTCP1 Human t-complex polypeptide 1 gene
106	137	PC010853D	D	4506660	Homo sapiens ribosomal protein L7a (RPL7A) mRNA
107	139	PC030968D	D	4507668	Homo sapiens tumor protein translationally-controlled 1 (TPT1) mRNA
138		PC031146D	D	8924228	NM_018636.1 Homo sapiens hypothetical protein PRO2987 (PRO2987)

Table 3

Name	Serial No.	Expression	Protein Gif	Classification	Domain	Domain description	Score	E	seq-f	seq-i
PC340	PC010139U	U	7657204		Homosapiens:acidic82[1]Daprotein[mmRNA](HSUJ55552)	mmRNA				
PC340	PC010139U	U	7657204		Ribosomal L2	Ribosomal Proteins L2	3.6	2.70E-01	197	217
PC342	PC010336U	U	7662580		Homosapiens:PR0064[1]protein[mmRNA](R000649)	mmRNA				
PC342	PC010336U	U	7662580							
PC341	PC010337U	U	6005814		Homosapiens:scirne[1]treanine[protein]kinase[mmRNA](NDR)	mmRNA				
PC341	PC010337U	U	6005814		pkinese	Protein kinase domain	221.1	8.30E-64	89	359
PC330	PC010433D	D	4827044	Down-regulated	Homosapiens:thyroid[1]hormone[receptor-associated]protein[mmRNA](R0A240)	Databank unit				
PC330	PC010433D	D	4827044		Na K-ATPase	Sodium / potassium ATPase beta chain	2.5	3.50E-01	224	239
PC330	PC010433D	D	4827044		Chal synt c	Chalcone and stilbene synthases, C-te	2.7	7.00E-01	1735	1752
PC339	PC010434U	U	4505375		A deuin	Adenosine-deaminase (ediasse) domain	1.2	9.10E-01	140	148
PC339	PC010434U	U	4505375		NM007499[1]Homosapiens:ogenin[1](chicken)homolog[1]					
PC339	PC010434U	U	4505375		fn3	Fibronectin type III domain	367.4	7.70E-108	954	1044
PC339	PC010434U	U	4505375		ig	Immunoglobulin domain	131.9	1.20E-40	355	412
PC339	PC010434U	U	4505375		Ribosomal L23	Ribosomal protein L23	2.9	9.40E-01	662	676
PC007	PC010839U	U	6912452		NM012289[1]Homosapiens:calg[1]ke[1]EGH-associated[protein]1[1](KFAA0192)					
PC007	PC010839U	U	6912452		Ketch	Ketch motif	271.7	5.10E-79	553	598
PC007	PC010839U	U	6912452		BTB	BTB/POZ domain	100.8	1.40E-27	61	179
PC007	PC010839U	U	6912452		PI3K p85B	PI3-kinase family, p85-binding domain	-21.1	8.20E-01	176	238
PC006	PC010849U	U	3978244		AF070067[4]Homosapiens:inhibitor[1]of[1]apoptosis[protein]1[1](M1HG)	mmRNA				
PC006	PC010849U	U	3978244		CARD	Caspase recruitment domain	125.1	6.80E-35	440	529
PC006	PC010849U	U	3978244		Zinc finger, C4 type (RING finger)	Zinc finger, C4 type (two domains)	3	7.40E-01	555	563
PC006	PC010849U	U	3978244		zf-C4	Zinc finger, C4 type (two domains)	3	7.40E-01	555	563
PC505	PC010853D	D	4506661	Down-regulated	Homosapiens:ribosomal[1]protein[1]87[1](R0197A)	mmRNA				
PC505	PC010853D	D	4506661		Ribosomal L7Ae	Ribosomal protein L7Ae/L30e/S12e/Gad	103.9	1.60E-28	122	216
PC505	PC010853D	D	4506661		Ribosomal L39	Ribosomal L39 protein	-8.6	2.60E-01	211	244
PC013	PC010853D	D	4557845		ribonuc red sm	Ribonucleotide reductase, small chain	598.8	1.70E-177	170	351
PC013	PC010957U	U	12003805		HSN4[1]7[1]Homosapiens:ribo[1]nuc[1]lease[1]M2[1]poly[peptide]1[1](R0M2)	mmRNA				
PC042	PC011348U	U	12003805		oxidored q1	NADH-1-Ubiquinone/plastoquinone (com)	22.9	9.30E-07	82	1108
PC353	PC020162U	U	4507165		NM003108[1]Homosapiens:nucleozin[1]gen[1]SP100[1](SP100)	mmRNA				
PC353	PC020162U	U	4507165							
PC350	PC020185U	U	7669503		NM010399[1]Homosapiens:lysosomal-associated[1]membrane[1]protein[1]2[1]					
PC350	PC020185U	U	7669503		Lump	Lysosome-associated membrane glycop	767.3	3.20E-228	44	410
PC358	PC020238D	D	4503091	Down-regulated	NM001893[1]Homosapiens:casein[1]kinase[1]gamma[1](GSNK1D)	mmRNA				
PC358	PC020238D	D	4503091		pkinese	Protein kinase domain	146.4	2.60E-41	9	239
PC367	PC020627U	U	14424570		Homosapiens:cione MG03166[1]MAGE[1]1[1]B34[1]					
PC367	PC020627U	U	14424570							
PC022	PC020728U	U	4503479		NM011960[1]Homosapiens:cell[1]ar[1]cyto[1]chrome[1]P450[1]2A6[1]					
PC022	PC020728U	U	4503479		EF1B	EF-1 guanine nucleotide exchange doma	189.4	3.00E-54	195	281
PC022	PC020728U	U	4503479		bZIP	bZIP transcription factor	10.1	1.30E-02	79	114
PC517	PC020741U	U	7657625		NM018393[1]Homosapiens:stand[1]ard[1]DNA-binding[protein]1[1](KFAA0192)					
PC517	PC020741U	U	7657625		Double stand-d DNA binding motif		125.1	6.10E-50	276	341



Table 3

PC039	PC040972U	U	4885133	Homosapiens	transcription factor	68.1	4.80E-19	2930	2962	
	PC040972U	U	4885133	bZIP	bZIP transcription factor	29.7	3.50E-06	2972	2992	
	PC040972U	U	4885133	M	M protein repeat	26.6	3.10E-05	2938	2948	
	PC040972U	U	4885133	KID repeat	KID repeat	13.2	8.80E-04	2810	2833	
	PC040972U	U	4885133	filament	Intermediate filament protein	-16.9	5.50E-02	1065	1157	
	PC040972U	U	4885133	Trp repressor	Trp repressor protein	28.7	9.90E-02	840	923	
	PC040972U	U	4885133	RNA pol L	RNA polymerases L / 13 to 16 kDa subunit	4.3	1.40E-01	2283	2338	
	PC040972U	U	4885133	Myosin tail	Myosin tail	-91.7	1.80E-01	2560	2797	
	PC040972U	U	4885133	DUF164	Uncharacterized ACR, COG1579	9	1.80E-01	2885	2928	
	PC040972U	U	4885133	HALZ	Homeobox associated leucine zipper	4.1	2.10E-01	2283	2294	
	PC040972U	U	4885133	OSCP	ATP synthase delta (OSCP) subunit	-40.4	3.10E-01	2440	2524	
	PC040972U	U	4885133	K-box	K-box region	-60.5	3.30E-01	2461	2730	
	PC040972U	U	4885133	HlyD	HlyD family secretion protein	3.9	4.00E-01	1888	1914	
	PC040972U	U	4885133	DUF38	Domain of unknown function DUF38	-179.4	4.20E-01	991	1223	
	PC040972U	U	4885133	dynamain 2	Dynamain central region	-4.4	4.70E-01	2201	2271	
	PC040972U	U	4885133	HRI	Hr1 repeat motif	-118.2	4.90E-01	2295	2547	
	PC040972U	U	4885133	Apolipoprotein	Apolipoprotein A1/A4/E family	3	5.60E-01	3068	3081	
	PC040972U	U	4885133	formyl transf	Formyl transferase	-227.4	6.50E-01	2028	2290	
	PC040972U	U	4885133	ERM	Ezrin/radixin/moesin family	1.3	7.20E-01	2418	2451	
	PC040972U	U	4885133	Tropomyosin	Tropomyosin	-107.4	7.40E-01	417	744	
	PC040972U	U	4885133	Borrelia orfA	Borrelia orfA	-89.6	7.90E-01	2844	2950	
	PC040972U	U	4885133	PFEMP	Plasmodium falciparum erythrocyte membrane protein 1	-41.4	8.40E-01	2891	2967	
	PC040972U	U	4885133	BglG antiterm	Transcriptional antiterminator bglG	-15.1	8.40E-01	566	624	
	PC040972U	U	4885133	TFIIIE beta	TFIIIE beta subunit core domain	-28.4	8.80E-01	2666	2793	
	PC040972U	U	4885133	TarH	Tar ligand binding domain homologue	-252.1	9.10E-01	2261	2712	
	PC040972U	U	4885133	FlitD	Flagellar hook-associated protein 2	-37	8.80E-14	50	295	
	PC041029U	U	4589596	Laminin N-term	Laminin N-terminal (Domain VI)	31.8	8.00E-07	297	341	
	PC041029U	U	4589596	Laminin EGF	Laminin EGF-like (Domains III and V)	3.9	5.20E-01	299	326	
	PC041029U	U	4589596	EGF	EGF-like domain	0.3	4.10E-02	33	142	
	PC041338U	U	8051621	NTP transf 2	Nucleotide transferase domain	-71.8	5.40E-01	2	162	
	PC041980U	U	6735452	HSAs024002	Homosapiens	245.9	2.90E-71	409	688	
	PC041980U	U	6735452	Down-regulated	Down-regulated	1.1	2.40E-01	471	493	
	PC042021D	D	4505987	SAM	SAM domain (Sterile alpha motif)	109.5	3.30E-30	711	774	
	PC042021D	D	4505987	Integrase DNA	DNA binding domain of integrase	28.1	1.10E-05	187	251	
	PC042021D	D	4505987	WHEP-TRS	WHEP-TRS domain	15.9	1.20E-04	123	137	
	PC042021D	D	4505987	DUF16	Protein of unknown function DUF16	-22.2	1.40E-01	90	167	
	PC042021D	D	4505987	bZIP	bZIP transcription factor	5.2	3.20E-01	205	244	
	PC042021D	D	4505987	STAT	STAT protein, all-alpha domain	-71.8	5.40E-01	2	162	
	PC050149U	U	2217931	pkase	Protein kinase domain	245.9	2.90E-71	409	688	
	PC050149U	U	2217931	A2M	Alpha-2-macroglobulin family	1.1	2.40E-01	471	493	

Table 3

PC050149U	U	2217931	DUF164	Uncharacterized ACR, COG1579	-99.2	5.10E-01	356	574	
PC050149U	U	2217931	Stathmin	Stathmin family	-22.4	8.40E-01	126	263	
PC087	PC050151U	6715600	NM002082	Homosapiens golgi autoantigenic subfamily 1					
PC050151U	U	6715600	GRIP	GRIP domain	77.2	1.70E-20	2171	2215	
PC050151U	U	6715600	M	M protein repeat	48.2	9.30E-12	2065	2085	
PC050151U	U	6715600	Involucrin	Involucrin repeat	14	4.20E-02	2005	2014	
PC050151U	U	6715600	Ribosomal L29	Ribosomal L29 protein	-7.7	8.80E-02	1263	1325	
PC050151U	U	6715600	DNA topoisomerase IV	DNA gyrase/topoisomerase IV, subunit	3.1	1.00E-01	1850	1882	
PC050151U	U	6715600	bZIP	bZIP transcription factor	6.7	1.20E-01	864	897	
PC050151U	U	6715600	DUF164	Uncharacterized ACR, COG1579	-89.1	1.20E-01	1559	1775	
PC050151U	U	6715600	Tropomyosin	Tropomyosin	3.4	1.50E-01	553	578	
PC050151U	U	6715600	Lipoprotein 7	Adhesin lipoprotein	-123	2.20E-01	725	1177	
PC050151U	U	6715600	DUF156	Uncharacterized BCR, COG1937	-9.6	3.90E-01	916	974	
PC050151U	U	6715600	UVR	UvrBuvrC motif	-3.8	5.00E-01	363	397	
PC050151U	U	6715600	ATP-synt ab C	ATP synthase alpha/beta chain, C term	-21.2	5.10E-01	381	486	
PC050151U	U	6715600	ICL	Isocitrate lyase family	-1.6	5.90E-01	1963	1980	
PC050151U	U	6715600	CagE, TrbE, VirB	CagE, TrbE, VirB family, component of	-86.1	6.30E-01	1091	1290	
PC050151U	U	6715600	Borrelia orfA	Borrelia orfA	-107.4	7.40E-01	1366	1698	
PC050151U	U	6715600	SEA	SEA domain	-10.6	7.80E-01	1177	1299	
PC050151U	U	6715600	DUF28	Domain of unknown function DUF28	-167.8	8.00E-01	1248	1422	
PC050151U	U	6715600	Bac DNA binding	Bacterial DNA-binding protein	3.4	8.20E-01	2103	2118	
PC050151U	U	6715600	MSG	Major surface glycoprotein	-6.3	9.60E-01	1576	1635	
PC050151U	U	6715600	Transposase 8	Transposase	-21.9	9.70E-01	1150	1228	
PC085	PC050296U	5453634	Homosapiens cyclin G1	Homosapiens cyclin G1					
PC050296U	U	5453634	GTP CDC	Cell division protein	5.7	6.60E-02	56	71	
PC050296U	U	5453634	ABC tran	ABC transporter	-66	1.80E-01	54	291	
PC050296U	U	5453634	SRP54	SRP54-type protein, GTPase domain	4.2	2.20E-01	53	74	
PC101	PC050620U	4504581	NM003641	Homosapiens interferon induced transmembrane protein					
PC050620U	U	4504581							
PC060	PC050832U	4503725	NM000801	Homosapiens K56 binding protein					
PC050832U	U	4503725	FKBP	FKBP-type peptidyl-prolyl cis-trans isom	179.2	6.30E-55	11	105	
PC076	PC051210U	4506057	NM002023	Homosapiens protein kinase C delta					
PC051210U	U	4506057	pk kinase	Protein kinase domain	303.4	1.50E-88	44	298	
PC083	PC051231U	4506601	Homosapiens ribosomal protein L14	Ribosomal protein L14	27.4	1.90E-08	299	330	
PC051231U	U	4506601	Ribosomal L14e	Ribosomal protein L14	120.1	2.20E-33	4	81	
PC90	PC051745D	4758752	Down-regulated	Ribosomal L27e protein family	-62	1.60E-01	3	120	
PC051745D	D	4758752	BIR	Inhibitor of Apoptosis domain	354.1	8.10E-104	281	346	
PC051745D	D	4758752	AAA	ATPase family associated with various	-45.7	4.00E-01	465	658	
PC051745D	D	4758752	Peptidase M29	Thermophilic metalloprotease (M29)	-0.4	6.20E-01	957	964	
PC051745D	D	4758752	ABC tran	ABC transporter	-72.9	6.40E-01	463	602	
PC051745D	D	4758752	NB-ARC	NB-ARC domain	1.5	7.70E-01	465	483	
PC100	PC052029U	5803219	Homosapiens serine protease inhibitor Kazal type 5	Serine protease inhibitor Kazal type 5					



Table 3

PC052029U	U	5803219	Kazal	Kazal-type serine protease inhibitor	172.5	3.70E-49	993	1046
PC052029U	U	5803219	RNA POL M 15K	RNA polymerases M15 Kd subunit	-7.8	6.40E-01	308	363
PC052029U	U	5803219	DnaJ CXXCXXG	DnaJ central domain (4 repeats)	-51.3	6.50E-01	751	823
PC052029U	U	5803219	Hirudin	Hirudin	-10.8	7.40E-01	380	441
PC093	PC052029U	U	Hirudin	Hirudin	-10.8	7.40E-01	380	441
PC052029U	U	641958	Myosin head	Myosin head (motor domain)	1495.3	0.00E+00	87	771
PC052029U	U	641958	Myosin tail	Myosin tail	788.7	1.20E-234	1073	1931
PC052029U	U	641958	M	M protein repeat	76.1	3.70E-20	1898	1918
PC052029U	U	641958	Myosin N	Myosin N-terminal SH3-like domain	70.1	2.40E-18	33	77
PC052029U	U	641958	IQ	IQ calmodulin-binding motif	22.3	5.90E-04	787	807
PC052029U	U	641958	Apolipoprotein	Apolipoprotein A1/A4/E family	-98.6	6.60E-02	1083	1318
PC052029U	U	641958	DUF164	Uncharacterized ACR, COG1579	-86.6	8.70E-02	1018	1250
PC052029U	U	641958	bZIP	bZIP transcription factor	7.2	8.80E-02	1788	1817
PC052029U	U	641958	Prismane	Prismane	-394.9	9.50E-02	171	425
PC052029U	U	641958	K-box	K-box region	-35.3	1.20E-01	965	1062
PC052029U	U	641958	Tub	Tub family	0.1	1.30E-01	742	748
PC052029U	U	641958	Tropomyosin	Tropomyosin	3.2	1.80E-01	1863	1898
PC052029U	U	641958	Lipoprotein 1	Borrelia lipoprotein	2.7	1.80E-01	1781	1809
PC052029U	U	641958	HR1	HR1 repeat motif	-0.6	2.10E-01	1034	1108
PC052029U	U	641958	HSP70	HSP70 protein	-414.1	2.20E-01	600	996
PC052029U	U	641958	OEP	Outer membrane efflux protein	-38.3	2.70E-01	1488	1684
PC052029U	U	641958	Involucrin	Involucrin repeat	10.5	3.30E-01	1823	1832
PC052029U	U	641958	kinesin	Kinesin motor domain	3.1	3.30E-01	1531	1548
PC052029U	U	641958	KE2	KE2 family protein	-47.4	4.00E-01	1062	1165
PC052029U	U	641958	HlyD	HlyD family secretion protein	-65	5.30E-01	863	1220
PC052029U	U	641958	NAP family	Nucleosome assembly protein (NAP)	2.5	5.40E-01	1107	1127
PC052029U	U	641958	UVR	UvrB/UvrC motif	-4.5	6.10E-01	1043	1077
PC052029U	U	641958	Birna VP5	Birnavirus VP5 protein	-36.2	7.30E-01	1232	1353
PC052029U	U	641958	BAR	BAR domain	-110.7	7.90E-01	1325	1534
PC052029U	U	641958	Transaldolase	Transaldolase	1	8.20E-01	1304	1317
PC052029U	U	641958	PV RdRp	Viral RNA dependent RNA polymerase	0.5	9.60E-01	1182	1210
PC129	PC060144D	D	Down-regulated	Down-regulated	0.5	9.60E-01	1182	1210
PC060144D	D	4758200	Plectin repeat	Plectin repeat	537.6	4.50E-159	2724	2768
PC060144D	D	4758200	bZIP	bZIP transcription factor	23.9	1.60E-06	1702	1740
PC060144D	D	4758200	spectrin	Spectrin repeat	24.2	1.60E-06	1060	1082
PC060144D	D	4758200	Myosin tail	Myosin tail	9.3	7.00E-03	1394	1416
PC060144D	D	4758200	M	M protein repeat	16.6	3.10E-02	1876	1896
PC060144D	D	4758200	G-gamma	GGL domain	5.8	9.60E-02	1892	1908
PC060144D	D	4758200	Exo70	Exo70 exocyst complex subunit	-263.9	1.90E-01	1779	2352
PC060144D	D	4758200	HALZ	Homeobox associated leucine zipper	7.4	2.90E-01	1382	1426
PC060144D	D	4758200	RNA pol B	RNA polymerase beta subunit	0.2	6.90E-01	2401	2413
PC060144D	D	4758200	HRI	HRI repeat motif	-6.6	7.40E-01	1844	1918
PC060144D	D	4758200	DNA pol B exo	DNA polymerase family B, exonuclease	1.5	7.50E-01	2713	2736
PC060144D	D	4758200	Troponin	Troponin	-34.7	7.50E-01	1666	1818





Table 3

PC080435D	D	4758808	RasGAP	GTase-activator protein for Ras-like	111.4	8.70E-31	348	520
PC080435D	D	4758808	PH	PH domain	19.9	1.90E-05	111	158
PC080435D	D	4758808	complex 49Kd	Respiratory-chain NADH dehydrogenase	8.4	3.90E-04	351	359
PC080435D	D	4758808	DEAD	DEAD/DEAH box helicase	8.8	3.70E-03	950	992
PC080435D	D	4758808	C2	C2 domain	5.8	4.60E-02	171	251
PC080435D	D	4758808	FLID	Flagellar hook-associated protein 2	242	3.50E-01	603	1101
PC216	PC080511U	4504191	NM40001791	Human sapiens:mutS(E6501)homolog(MSH6)	132.1	3.30E-94	1054	1316
	PC080511U	4504191	MutS C	DNA mismatch repair proteins, mutS fa	132.1	3.30E-94	1054	1316
	PC080511U	4504191	MutS N	MutS family, N-terminal putative DNA	216.6	2.00E-62	409	977
	PC080511U	4504191	PWWP	PWWP domain	127.1	1.60E-35	89	162
	PC080511U	4504191	SNF	Sodium:neurotransmitter symporter fam	1.3	7.30E-01	753	768
	PC080511U	4504191	Luteo ORF3	Luteovirus (ORF3) RNA-directed RNA-	0.3	8.60E-01	1304	1330
PC274	PC080742U	4507187	NM40031251	Human sapiens:small protein(B) (corrin)	57	2.10E-14	1	87
	PC080742U	4507187	Comifin	Comifin (SPRR) family	57	2.10E-14	1	87
PC299	PC090230U	3252911	AF056322	Human sapiens:SP100-HMG nuclear autoantigen (SP100)mirNA	180	2.10E-51	595	676
	PC090230U	3252911	SAND	SAND domain	180	2.10E-51	595	676
	PC090230U	3252911	HMG box	HMG (high mobility group) box	118.3	7.70E-33	769	837
PC302	PC090233U	4504193	Human sapiens:general transcription factor TFIIB repeat	transcription factor TFIIB repeat	231.1	8.60E-67	215	285
	PC090233U	4504193	cyclin	Cyclin, N-terminal domain	26.6	8.30E-02	94	207
	PC090233U	4504193	Down-regulated	Down-regulated	534.3	6.50E-187	3	308
PC316	PC090622D	4506859	Human sapiens:H2-K binding factor 24 (H2KBF24)mirNA	55.5	6.20E-14	275	365	
PC315	PC090625U	7706216	Human sapiens:H2-K binding factor 24 (H2KBF24)mirNA	55.5	6.20E-14	275	365	
	PC090625U	7706216	TIG	IPT/TIG domain	11.7	2.40E-03	165	221
	PC090625U	7706216	ig	Immunoglobulin domain	11.7	2.40E-03	165	221
PC310	PC090677D	307218	Human sapiens:MH2H domain	200.3	1.60E-57	275	311	
	PC090677D	307218	WD40	WD domain, G-beta repeat	200.3	1.60E-57	275	311
PC239	PC090722D	7670748	Human sapiens:UDDP-glucose 6-phosphate dehydrogenase precursor mirNA	237.8	8.20E-69	4	175	
PC230	PC090734U	4503473	Human sapiens:UDDP-glucose 6-phosphate dehydrogenase precursor mirNA	237.8	8.20E-69	4	175	
	PC090734U	4503473	GTP EFTU	Elongation factor Tu GTP binding domain	237.8	8.20E-69	4	175
	PC090734U	4503473	GTP EFTU D3	Elongation factor Tu C-terminal domain	201.1	8.80E-58	269	378
	PC090734U	4503473	GTP EFTU D2	Elongation factor Tu domain 2	98.6	1.50E-27	187	263
PC220	PC090754U	4503473	Human sapiens:GTP EFTU D2	Elongation factor Tu domain 2	98.6	1.50E-27	187	263
	PC090754U	4503473	Human sapiens:GTP EFTU D2	Elongation factor Tu domain 2	98.6	1.50E-27	187	263
	PC090788D	5031639	Human sapiens:GTP EFTU D2	Elongation factor Tu domain 2	98.6	1.50E-27	187	263
	PC090788D	5031639	Human sapiens:GTP EFTU D2	Elongation factor Tu domain 2	98.6	1.50E-27	187	263
PC233	PC090842U	4557032	Human sapiens:lactate dehydrogenase B (LDHB)mirNA	297	1.20E-86	164	333	
	PC090842U	4557032	ldh C	lactate/malate dehydrogenase, alpha/beta	297	1.20E-86	164	333
	PC090842U	4557032	ldh	lactate/malate dehydrogenase, NAD bind	284.4	7.30E-83	19	162
PC236	PC091028U	7662426	Human sapiens:KlA0976 protein (KlA0976)mirNA	37	8.80E-14	50	295	
	PC091028U	7662426	laminin Nterm	Laminin N-terminal (Domain VI)	37	8.80E-14	50	295
	PC091028U	7662426	laminin EGF	Laminin EGF-like (Domains III and V)	31.8	8.00E-07	297	341
	PC091028U	7662426	EGF	EGF-like domain	3.9	5.20E-01	299	326
PC324	PC091425U	4732026	Human sapiens:angiotensin converting enzyme precursor	341.5	0.00E+00	634	1228	
	PC091425U	4732026	Peptidase M2	Angiotensin-converting enzyme	341.5	0.00E+00	634	1228
	PC091425U	4732026	HupF HvpC	HupF/HvpC family	-34	5.00E-01	1231	1286

Table 3

PC091425U	U	4732026	Phosphoprotein	Vesiculovirus phosphoprotein	0.1	7.10E-01	596	607
PC091425U	U	4732026	MM CoA mutase	Methylmalonyl-CoA mutase	0.9	7.70E-01	192	221
PC400	U	5803092	Homoglycylsine aminopeptidase	Homoglycylsine aminopeptidase (G125 associated with MNPEP) (H18N46)				
PC091527U	U	5803092	Peptidase M24	Peptidase M24	319	2.80E-93	159	404
PC091527U	U	5803092	PBP GOBP family	PBP GOBP family	-51.4	9.10E-01	127	254
PC407	U	7188647	ATP synthase	ATP synthase (NAG20) (H18N46)				
PC405	U	31092	ATP synthase	ATP synthase (NAG20) (H18N46)				
PC091853U	U	31092	GTP EFTU	Elongation factor Tu GTP binding domain	378.7	3.00E-111	5	239
PC091853U	U	31092	GTP EFTU D3	Elongation factor Tu C-terminal domain	212.7	3.00E-61	333	442
PC091853U	U	31092	GTP EFTU D2	Elongation factor Tu domain 2	100.7	3.80E-28	251	327
PC091853U	U	31092	pyr. redox	Pyridine nucleotide-disulphide oxidoreductase	-99.3	6.10E-01	9	286
PC091853U	U	31092	ATP-bind	Conserved hypothetical ATP binding protein	-138.3	9.80E-01	9	182
PC402	U	4757810	ATP synthase	ATP synthase (H18N46)				
PC091888U	U	4757810	ATP-synt ab	ATP synthase alpha/beta family, nucleosome	554.9	2.80E-164	138	421
PC091888U	U	4757810	ATP-synt ab C	ATP synthase alpha/beta chain, C-terminal	140.6	1.40E-39	423	531
PC091888U	U	4757810	ATP-synt ab N	ATP synthase alpha/beta family, beta-b	76.5	2.80E-20	67	135
PC091888U	U	4757810	FwdE	Tungsten formylmethanofuran dehydrogenase	-97.9	9.90E-01	230	408
PC401	U	8922824	zF-C2H2	Zinc finger, C2H2 type	455.9	1.80E-134	457	479
PC092004U	U	8922824	zF-BED	BED zinc finger	4.8	2.00E-02	246	284
PC092004U	U	8922824	LIM	LIM domain	-16.7	2.30E-01	431	483
PC092004U	U	8922824	BolA	BolA-like protein	-24.5	2.70E-01	100	157
PC092004U	U	8922824	zF-MIZ	MIZ zinc finger	-21.1	4.70E-01	354	412
PC092004U	U	8922824	TFIIS	Transcription factor S-II (TFIIS)	-6.9	4.90E-01	289	327
PC092004U	U	8922824	PHD	PHD-finger	-20.8	7.90E-01	122	185
PC092004U	U	8922824	zF-ANI	ANI-like Zinc finger	-11.8	8.20E-01	123	169
PC406	U	4505635	cadherin	cadherin (H18N46)				
PC092052U	U	4505635	Adeno E3 CR2	Adenovirus E3 region protein CR2	-2.9	2.90E-01	873	912
PC092052U	U	4505635	Herpes gE	Alphaherpesvirus glycoprotein E	-257.7	3.90E-01	552	948
PC092052U	U	4505635	CBD 6	Cellulose binding domain	-23.5	6.10E-01	627	786
PC279	U	5733684	trypsin	Trypsin	277	1.90E-88	30	245
PC100113U	U	5733684	toxin 4	toxin 4	-3.3	4.70E-01	200	239
PC285	U	13272790	oxidored q1	oxidored q1 (H18N46)				
PC100356U	U	13272790	oxidored q2 N	oxidored q2 N	344.3	6.80E-101	112	404
PC100356U	U	13272790	sugar tr	Sugar (and other) transporter	-201.8	5.80E-61	1	109
PC100356U	U	13272790	DebD	Cytochrome C biogenesis protein trans	-101.5	7.50E-01	126	305
PC100356U	U	13272790	DUF6	Integral membrane protein DUF6	-29.6	9.80E-01	286	408
PC294	U	4502981	COX4	Cytochrome c oxidase subunit IV	242.1	4.00E-70	26	169
PC10428U	U	182851	COX4	Cytochrome c oxidase subunit IV	242.1	4.00E-70	26	169
PC10430U	U	182851	COX4	Cytochrome c oxidase subunit IV	242.1	4.00E-70	26	169
PC10430U	U	182851	COX4	Cytochrome c oxidase subunit IV	242.1	4.00E-70	26	169



## SEQUENCE LISTING

&lt;110&gt; OriGene Technologies

&lt;120&gt; Prostate Cancer Expression Profiles

&lt;130&gt; 9U 206 PCT

&lt;150&gt; US 60/281,732

&lt;151&gt; 2001-04-06

&lt;150&gt; US 60/281,731

&lt;151&gt; 2001-04-06

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<212> DNA
<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

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<211> 1488
<212> DNA
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<212> DNA  
<213> Homo sapiens

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 <211> 1622  
 <212> DNA  
 <213> Homo sapiens

<400> 15



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<211> 7694
<212> DNA
<213> Homo sapiens

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aaagcaccga agattcagcg tcttgttact ccacgtgtcc tgcagcacaac acggcggcgt 600  
attgctctga agcaacagcg taccaagaaa aataaagaag aggctgcaga atatgctaaa 660  
cttttgccca agagaatgaa ggaggctaag gagaagcgcc aggaacaaat tgcgaagaga 720  
cgcagacttt cctctctcgc agcttctact tctaagtctg aatccagtca gaaatagatt 780  
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<210> 25  
<211> 1434  
<212> DNA  
<213> Homo sapiens

<400> 25  
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tactacgacc tcgaaaaaga tgtgaaacag tttgttagga gaaaggacag tggctcgtgt 180  
gttaaaaaaa tccgagaaat gcagaagttc cttggattgg aggtgacggg gaagctggac 240  
tccgacactc tggaggtgat gcgcaagccc aggtgtggag ttcttgacgt tggtcacttc 300  
agaacctttc ctggcatccc gaagtggagg aaaaccaccc ttacatacag gattgtgaat 360  
tatacaccag atttgccaaa agatgtgtgt gattctgctg ttgagaaagc tctgaaagtc 420  
tgggaagagg tgactccact cacattctcc aggtgtgatg aaggagaggc tgatataatg 480  
atctcttttg cagttagaga acatggagac ttttaccctt ttgatggacc tggaaatgtt 540  
ttggcccatg cctatgcccc tgggccaggg attaattggag atgccactt tgatgatgat 600  
gaacaatgga caaaggatag aacagggacc aatttatttc tcgttgctgc tcatgaaatt 660  
ggccactccc tgggtctctt tcaactcagc aacactgaag ctttgatgta cccactctat 720

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cactcactca cagacctgac tcggttccgc ctgacccaaay alyavataaa tyytallcag 780
tcctcttatg gacctcccc tgactcccct gagaccccc tggtaccac ggaacctgtc 840
cctccagaac ctgggacgcc agccaactgt gatcctgctt tgtcctttga tgctgtcagc 900
actctgaggg gagaaatcct gatctttaa gacaggcact tttggcgcaa atccctcagg 960
aagcttgaac ctgaattgca tttgatctct tcattttggc catctcttcc ttcaggcgtg 1020
gatgccgcat atgaagttac tagcaaggac ctcgttttca tttttaagg aaatcaattc 1080
tgggccatca gaggaatga ggtacgagct ggatacccaa gaggcacca caccctaggt 1140
ttccctccaa ccgtgaggaa aatcgatgca gccattttctg ataaggaaaa gaacaaaaca 1200
tatttctttg tagaggacaa atactggaga tttgatgaga agagaaattc catggagcca 1260
ggctttccca agcaaatagc tgaagacttt ccagggattg actcaaagat tgatgctgtt 1320
tttgaagaat ttgggttctt ttatttcttt actggatctt cacagttgga gtttgacca 1380
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<210> 26
<211> 540
<212> DNA
<213> Homo sapiens

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ttacggggaa gaccatcacc ctcgaggttg aacctcgga tacgatagaa aatgtaaagg 120
ccaagatcca ggataaggaa ggaattcctc ctgatcagca gagactgac tttgctggca 180
agcagctaga agatggacgt actttgtctg actacaatat tcaaaaggag tctactctt 240
atcttgtgtt gagacttctg ggtggtgcta agaaaaggaa gaagaagtct tacaccact 300
ccaagaagaa taagcacaag agaaagaagg ttaagctggc tgcctgaaa tattataagg 360
tgatgagaa tggcaaaatt agtcgccttc gtcgagagt cccttctgat gaatgtggtg 420
ctggggtgtt tatggcaagt cactttgaca gacattattg tggcaaatgt tgtctgactt 480
actgtttcaa caaacagaa gacaagtaac tgtatgagtt aataaaagac atgaactaac 540

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<210> 27
<211> 2400
<212> DNA
<213> Homo sapiens

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ggaatacaag caagaaagaa cttattcaac aaccaaggaa atgccagccc tcctgcagga 180
cccagcaatg tacctaagtt tgggtcccca aagccacctg tggcagtcaa accttcttct 240
gaggaaaagc ctgacaagga acccaagccc ccgtttctaa agccactgg agcaggccaa 300
agattcgga caccagccag cttgaccacc agagacccc aggcgaaagt gggatttctg 360
aaacctgtag gccccagcc catcaacttg ccaagaag attccaaacc tacatttccc 420
tggcctctg gaaacaagcc atctctcac agtgtaaacc aagaccatga cttaaagcca 480
ctaggccga aatctgggcc tactctcca acctcagaaa atgaacagaa gcaagcgttt 540
cccaaattga ctggggttaa agggaaattt atgtcagcat cacaagatct tgaacccaag 600
cccctcttcc ccaaacccgc ctttgccag aagccgcccc taagtaccga gaactccat 660
gaagacgaaa gccccatgaa gaatgtgtct tcacaaaag ggtcccagc tcccctggga 720

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gtcagggtcca aaagcgcccc tttaaaacca gcaagggaag actcagaaaa taaagaccat 780  
 gcaggggaga tttcaagttt gccctttcct ggagtgggtt tgaaacctgc tgcgagcagg 840  
 ggagggcctag gtctctccaa aaatggtgaa gaaaaaaagg aagataggaa gatagatgct 900  
 gctaagaaca ccttcagag caaaataaat caggaagagt tggcctcagg gactcctcct 960  
 gccaggttcc ctaaggcccc ttctaagctg acagtggggg ggccatgggg ccaaagtcag 1020  
 gaaaaggaaa agggagacaa gaattcagcc accccgaaac agaagccatt gcctcccttg 1080  
 tttaccttg gtccacctcc accaaaacc aacagaccac caaatgttga cctgacgaaa 1140  
 ttccacaaaa cctcttcttg aaacagtact agcaaaggcc agacgtctta ctcaacaact 1200  
 tccctgccac cacctccacc atcccatcg gccagccaac caccattgcc agcatctcac 1260  
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 ctatagtagg aacaagacag tgaaggagaa acatatgaag acatagaagc atccaaagaa 1440  
 agagagaaga aaagggaaaa ggaagaaaag aagaggttag agctggagaa aaaggaacag 1500  
 aaagagaaag aaaagaaaga acaagaaata aagaagaaat ttaactaac aggccctatt 1560  
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 ttgggcagaa cagcaagggg tcatatggc tatattaaa caactgctgt agagattgac 1740  
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 gaccaagaag tatatgatga tgttcagag caggatgata ttagcagcca cagtcagagt 1860  
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 gaagatgctg atgatgggtt ccctgctcct cctaaacaat tggacatggg agatgaagtt 1980  
 tacgatgatg tggatacctc tgatttcct gtttcacag cagagatgag tcaaggaaact 2040  
 aattttgaa aagctaagac agaagaaaag gaccttaaga agctaaaaa gcaggaaaaa 2100  
 gaagaaaaag acttcaggaa aaaatttaa tatgatggtg aaattagagt cctatattca 2160  
 actaaagtta caacttccat aacttctaaa aagtggggaa ccagagatct acaggtaaaa 2220  
 cctggtgaat ctctagaagt tatacaaacc acagatgaca caaaagtct ctgcagaaat 2280  
 gaagaaggga aatatggtta tgtccttcg agttacctag cggacaatga tggagagatc 2340  
 tatgatgata ttgctgatg ctgcacttat gacaatgact agcactcaac tttggtcatt 2400

<210> 28  
 <211> 794  
 <212> DNA  
 <213> Homo sapiens

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 ggcggcagga agcgggacgc ccgagagga ggaggtacct gctggggagg cagcggcctc 180  
 gcagccccag gcccacga gtgtgcctgg ggctcgtctc tcgaggttgc ctctggcgcg 240  
 agtgaaggcc ttggtgaagg cagatccga cgtgacgcta gcgggacagg aagccatctt 300  
 cattctggca cgagccgagg aactgtttgt ggagaccatt gcaaaagatg cctactgttg 360  
 cgctcagcag ggaagaaaga aaacccttca gaggagagac ttggataatg caatagaagc 420  
 tgtggatgaa ttgcttttc tgaaggtac tttagattga ttgccgagcg gggcagtttt 480



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Gly Gly Phe Glu Ala Tyr Thr Gly Gly Leu Glu Leu Met Glu Gly Arg
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Lys Gln Phe Asp Glu Leu Cys Ile Pro Phe Val Val Ile Pro Ala Thr
      515      520      525
Val Ser Asn Asn Val Pro Gly Ser Asp Phe Ser Val Gly Ala Asp Thr
      530      535      540
Ala Leu Asn Thr Ile Cys Thr Thr Cys Asp Arg Ile Lys Gln Ser Ala
      545      550      555      560
Ala Gly Thr Lys Arg Arg Val Phe Ile Ile Glu Thr Met Gly Gly Tyr
      565      570      575
Cys Gly Tyr Leu Ala Thr Met Ala Gly Leu Ala Ala Gly Ala Asp Ala
      580      585      590
Ala Tyr Ile Phe Glu Glu Pro Phe Thr Ile Arg Asp Leu Gln Ala Asn
      595      600      605
Val Glu His Leu Val Gln Lys Met Lys Thr Thr Val Lys Arg Gly Leu
      610      615      620
Val Leu Arg Asn Glu Lys Cys Asn Glu Asn Tyr Thr Thr Asp Phe Ile
      625      630      635      640
Phe Asn Leu Tyr Ser Glu Glu Gly Lys Gly Ile Phe Asp Ser Arg Lys
      645      650      655
Asn Val Leu Gly His Met Gln Gln Gly Gly Ser Pro Thr Pro Phe Asp
      660      665      670
Arg Asn Phe Ala Thr Lys Met Gly Ala Lys Ala Met Asn Trp Met Ser
      675      680      685
Gly Lys Ile Lys Glu Ser Tyr Arg Asn Gly Arg Ile Phe Ala Asn Thr
      690      695      700
Pro Asp Ser Gly Cys Val Leu Gly Met Arg Lys Arg Ala Leu Val Phe
      705      710      715      720
Gln Pro Val Ala Glu Leu Lys Asp Gln Thr Asp Phe Glu His Arg Ile
      725      730      735
Pro Lys Glu Gln Trp Trp Leu Lys Leu Arg Pro Ile Leu Lys Ile Leu
      740      745      750
Ala Lys Tyr Glu Ile Asp Leu Asp Thr Ser Asp His Ala His Leu Glu
      755      760      765
His Ile Thr Arg Lys Arg Ser Gly Glu Ala Ala Val
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<210> 110
<211> 1403
<212> PRT
<213> Homo sapiens

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&lt;400&gt; 110

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Gln Leu Ala Lys Glu Leu Glu Glu Glu Gln Lys Glu Arg Ala Lys  
35 40 45

Met Gln Lys Gly Tyr Asn Ser Gln Met Arg Ser Glu Ala Lys Arg Leu  
50 55 60

Lys Thr Phe Val Thr Tyr Glu Pro Tyr Ser Ser Trp Ile Pro Gln Glu  
65 70 75 80

Met Ala Ala Ala Gly Phe Tyr Phe Thr Gly Val Lys Ser Gly Ile Gln  
85 90 95

Cys Phe Cys Cys Ser Leu Ile Leu Phe Gly Ala Gly Leu Thr Arg Leu  
100 105 110

Pro Ile Glu Asp His Lys Arg Phe His Pro Asp Cys Gly Phe Leu Leu  
115 120 125

Asn Lys Asp Val Gly Asn Ile Ala Lys Tyr Asp Ile Arg Val Lys Asn  
130 135 140

Leu Lys Ser Arg Leu Arg Gly Gly Lys Met Arg Tyr Gln Glu Glu Glu  
145 150 155 160

Ala Arg Leu Ala Ser Phe Arg Asn Trp Pro Phe Tyr Val Gln Gly Ile  
165 170 175

Ser Pro Cys Val Leu Ser Glu Ala Gly Phe Val Phe Thr Gly Lys Gln  
180 185 190

Asp Thr Val Gln Cys Phe Ser Cys Gly Gly Cys Leu Gly Asn Trp Glu  
195 200 205

Glu Gly Asp Asp Pro Trp Lys Glu His Ala Lys Trp Phe Pro Lys Cys  
210 215 220

Glu Phe Leu Arg Ser Lys Lys Ser Ser Glu Glu Ile Thr Gln Tyr Ile  
225 230 235 240

Gln Ser Tyr Lys Gly Phe Val Asp Ile Thr Gly Glu His Phe Val Asn  
245 250 255

Ser Trp Val Gln Arg Glu Leu Pro Met Ala Ser Ala Tyr Cys Asn Asp  
260 265 270

Ser Ile Phe Ala Tyr Glu Glu Leu Arg Leu Asp Ser Phe Lys Asp Trp  
275 280 285

Pro Arg Glu Ser Ala Val Gly Val Ala Ala Leu Ala Lys Ala Gly Leu  
290 295 300

Phe Tyr Thr Gly Ile Lys Asp Ile Val Gln Cys Phe Ser Cys Gly Gly  
 305 310 315 320  
 Cys Leu Glu Lys Trp Gln Glu Gly Asp Asp Pro Leu Asp Asp His Thr  
 325 330 335  
 Arg Cys Phe Pro Asn Cys Pro Phe Leu Gln Asn Met Lys Ser Ser Ala  
 340 345 350  
 Glu Val Thr Pro Asp Leu Gln Ser Arg Gly Glu Leu Cys Glu Leu Leu  
 355 360 365  
 Glu Thr Thr Ser Glu Ser Asn Leu Glu Asp Ser Ile Ala Val Gly Pro  
 370 375 380  
 Ile Val Pro Glu Met Ala Gln Gly Glu Ala Gln Trp Phe Gln Glu Ala  
 385 390 395 400  
 Lys Asn Leu Asn Glu Gln Leu Arg Ala Ala Tyr Thr Ser Ala Ser Phe  
 405 410 415  
 Arg His Met Ser Leu Leu Asp Ile Ser Ser Asp Leu Ala Thr Asp His  
 420 425 430  
 Leu Leu Gly Cys Asp Leu Ser Ile Ala Ser Lys His Ile Ser Lys Pro  
 435 440 445  
 Val Gln Glu Pro Leu Val Leu Pro Glu Val Phe Gly Asn Leu Asn Ser  
 450 455 460  
 Val Met Cys Val Glu Gly Glu Ala Gly Ser Gly Lys Thr Val Leu Leu  
 465 470 475 480  
 Lys Lys Ile Ala Phe Leu Trp Ala Ser Gly Cys Cys Pro Leu Leu Asn  
 485 490 495  
 Arg Phe Gln Leu Val Phe Tyr Leu Ser Leu Ser Ser Thr Arg Pro Asp  
 500 505 510  
 Glu Gly Leu Ala Ser Ile Ile Cys Asp Gln Leu Leu Glu Lys Glu Gly  
 515 520 525  
 Ser Val Thr Glu Met Cys Met Arg Asn Ile Ile Gln Gln Leu Lys Asn  
 530 535 540  
 Gln Val Leu Phe Leu Leu Asp Asp Tyr Lys Glu Ile Cys Ser Ile Pro  
 545 550 555 560  
 Gln Val Ile Gly Lys Leu Ile Gln Lys Asn His Leu Ser Arg Thr Cys  
 565 570 575  
 Leu Leu Ile Ala Val Arg Thr Asn Arg Ala Arg Asp Ile Arg Arg Tyr  
 580 585 590  
 Leu Glu Thr Ile Leu Glu Ile Lys Ala Phe Pro Phe Tyr Asn Thr Val  
 595 600 605  
 Cys Ile Leu Arg Lys Leu Phe Ser His Asn Met Thr Arg Leu Arg Lys  
 610 615 620

Phe Met Val Tyr Phe Gly Lys Asn Gln Ser Leu Gln Lys Ile Gln Lys  
 625 630 635 640  
 Thr Pro Leu Phe Val Ala Ala Ile Cys Ala His Trp Phe Gln Tyr Pro  
 645 650 655  
 Phe Asp Pro Ser Phe Asp Asp Val Ala Val Phe Lys Ser Tyr Met Glu  
 660 665 670  
 Arg Leu Ser Leu Arg Asn Lys Ala Thr Ala Glu Ile Leu Lys Ala Thr  
 675 680 685  
 Val Ser Ser Cys Gly Glu Leu Ala Leu Lys Gly Phe Phe Ser Cys Cys  
 690 695 700  
 Phe Glu Phe Asn Asp Asp Asp Leu Ala Glu Ala Gly Val Asp Glu Asp  
 705 710 715 720  
 Glu Asp Leu Thr Met Cys Leu Met Ser Lys Phe Thr Ala Gln Arg Leu  
 725 730 735  
 Arg Pro Phe Tyr Arg Phe Leu Ser Pro Ala Phe Gln Glu Phe Leu Ala  
 740 745 750  
 Gly Met Arg Leu Ile Glu Leu Leu Asp Ser Asp Arg Gln Glu His Gln  
 755 760 765  
 Asp Leu Gly Leu Tyr His Leu Lys Gln Ile Asn Ser Pro Met Met Thr  
 770 775 780  
 Val Ser Ala Tyr Asn Asn Phe Leu Asn Tyr Val Ser Ser Leu Pro Ser  
 785 790 795 800  
 Thr Lys Ala Gly Pro Lys Ile Val Ser His Leu Leu His Leu Val Asp  
 805 810 815  
 Asn Lys Glu Ser Leu Glu Asn Ile Ser Glu Asn Asp Asp Tyr Leu Lys  
 820 825 830  
 His Gln Pro Glu Ile Ser Leu Gln Met Gln Leu Leu Arg Gly Leu Trp  
 835 840 845  
 Gln Ile Cys Pro Gln Ala Tyr Phe Ser Met Val Ser Glu His Leu Leu  
 850 855 860  
 Val Leu Ala Leu Lys Thr Ala Tyr Gln Ser Asn Thr Val Ala Ala Cys  
 865 870 875 880  
 Ser Pro Phe Val Leu Gln Phe Leu Gln Gly Arg Thr Leu Thr Leu Gly  
 885 890 895  
 Ala Leu Asn Leu Gln Tyr Phe Phe Asp His Pro Glu Ser Leu Ser Leu  
 900 905 910  
 Leu Arg Ser Ile His Phe Pro Ile Arg Gly Asn Lys Thr Ser Pro Arg  
 915 920 925  
 Ala His Phe Ser Val Leu Glu Thr Cys Phe Asp Lys Ser Gln Val Pro  
 930 935 940

Thr Ile Asp Gln Asp Tyr Ala Ser Ala Phe Glu Pro Met Asn Glu Trp  
 945 950 955 960  
 Glu Arg Asn Leu Ala Glu Lys Glu Asp Asn Val Lys Ser Tyr Met Asp  
 965 970 975  
 Met Gln Arg Arg Ala Ser Pro Asp Leu Ser Thr Gly Tyr Trp Lys Leu  
 980 985 990  
 Ser Pro Lys Gln Tyr Lys Ile Pro Cys Leu Glu Val Asp Val Asn Asp  
 995 1000 1005  
 Ile Asp Val Val Gly Gln Asp Met Leu Glu Ile Leu Met Thr Val  
 1010 1015 1020  
 Phe Ser Ala Ser Gln Arg Ile Glu Leu His Leu Asn His Ser Arg  
 1025 1030 1035  
 Gly Phe Ile Glu Ser Ile Arg Pro Ala Leu Glu Leu Ser Lys Ala  
 1040 1045 1050  
 Ser Val Thr Lys Cys Ser Ile Ser Lys Leu Glu Leu Ser Ala Ala  
 1055 1060 1065  
 Glu Gln Glu Leu Leu Leu Thr Leu Pro Ser Leu Glu Ser Leu Glu  
 1070 1075 1080  
 Val Ser Gly Thr Ile Gln Ser Gln Asp Gln Ile Phe Pro Asn Leu  
 1085 1090 1095  
 Asp Lys Phe Leu Cys Leu Lys Glu Leu Ser Val Asp Leu Glu Gly  
 1100 1105 1110  
 Asn Ile Asn Val Phe Ser Val Ile Pro Glu Glu Phe Pro Asn Phe  
 1115 1120 1125  
 His His Met Glu Lys Leu Leu Ile Gln Ile Ser Ala Glu Tyr Asp  
 1130 1135 1140  
 Pro Ser Lys Leu Val Lys Leu Ile Gln Asn Ser Pro Asn Leu His  
 1145 1150 1155  
 Val Phe His Leu Lys Cys Asn Phe Phe Ser Asp Phe Gly Ser Leu  
 1160 1165 1170  
 Met Thr Met Leu Val Ser Cys Lys Lys Leu Thr Glu Ile Lys Phe  
 1175 1180 1185  
 Ser Asp Ser Phe Phe Gln Ala Val Pro Phe Val Ala Ser Leu Pro  
 1190 1195 1200  
 Asn Phe Ile Ser Leu Lys Ile Leu Asn Leu Glu Gly Gln Gln Phe  
 1205 1210 1215  
 Pro Asp Glu Glu Thr Ser Glu Lys Phe Ala Tyr Ile Leu Gly Ser  
 1220 1225 1230  
 Leu Ser Asn Leu Glu Glu Leu Ile Leu Pro Thr Gly Asp Gly Ile

1235                      1240                      1245  
 Tyr Arg Val Ala Lys Leu Ile Ile Gln Gln Cys Gln Gln Leu His  
 1250                      1255                      1260  
 Cys Leu Arg Val Leu Ser Phe Phe Lys Thr Leu Asn Asp Asp Ser  
 1265                      1270                      1275  
 Val Val Glu Ile Ala Lys Val Ala Ile Ser Gly Gly Phe Gln Lys  
 1280                      1285                      1290  
 Leu Glu Asn Leu Lys Leu Ser Ile Asn His Lys Ile Thr Glu Glu  
 1295                      1300                      1305  
 Gly Tyr Arg Asn Phe Phe Gln Ala Leu Asp Asn Met Pro Asn Leu  
 1310                      1315                      1320  
 Gln Glu Leu Asp Ile Ser Arg His Phe Thr Glu Cys Ile Lys Ala  
 1325                      1330                      1335  
 Gln Ala Thr Thr Val Lys Ser Leu Ser Gln Cys Val Leu Arg Leu  
 1340                      1345                      1350  
 Pro Arg Leu Ile Arg Leu Asn Met Leu Ser Trp Leu Leu Asp Ala  
 1355                      1360                      1365  
 Asp Asp Ile Ala Leu Leu Asn Val Met Lys Glu Arg His Pro Gln  
 1370                      1375                      1380  
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 1385                      1390                      1395  
 Pro Ile Ile Gln Lys  
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 20                      25                      30  
 Phe Asp Cys Gln Ser Pro Thr Ser Pro Phe Met Gly Ser Leu Arg Ala  
 35                      40                      45  
 Leu His Leu Val Glu Asp Leu Arg Gly Leu Leu Glu Met Met Glu Thr  
 50                      55                      60  
 Asp Glu Lys Glu Gly Leu Arg Cys Gln Ile Pro Asp Ser Thr Ala Glu  
 65                      70                      75                      80  
 Thr Leu Val Glu Trp Leu Gln Ser Gln Met Thr Asn Gly His Leu Pro  
 85                      90                      95  
 Gly Asn Gly Asp Val Tyr Gln Glu Arg Leu Ala Arg Leu Glu Asn Asp

100	105	110
Lys Glu Ser Leu Val Leu Gln Val Ser Val Leu Thr Asp Gln Val Glu 115 120 125		
Ala Gln Gly Glu Lys Ile Arg Asp Leu Glu Phe Cys Leu Glu Glu His 130 135 140		
Arg Glu Lys Leu Asn Ala Thr Glu Glu Met Leu Gln Gln Glu Leu Leu 145 150 155 160		
Ser Arg Thr Ser Leu Glu Thr Gln Lys Leu Asp Leu Met Ala Glu Ile 165 170 175		
Ser Asn Leu Lys Leu Lys Leu Thr Ala Val Glu Lys Asp Arg Leu Asp 180 185 190		
Tyr Glu Asp Lys Phe Arg Asp Thr Glu Gly Leu Ile Gln Glu Ile Asn 195 200 205		
Asp Leu Arg Leu Lys Val Ser Glu Met Asp Ser Glu Arg Leu Gln Tyr 210 215 220		
Glu Lys Lys Leu Lys Ser Thr Lys Asp Glu Leu Ala Ser Leu Lys Glu 225 230 235 240		
Gln Leu Glu Glu Lys Glu Ser Glu Val Lys Arg Leu Gln Glu Lys Leu 245 250 255		
Val Cys Lys Met Lys Gly Glu Gly Val Glu Ile Val Asp Arg Asp Glu 260 265 270		
Asn Phe Lys Lys Lys Leu Lys Glu Lys Asn Ile Glu Val Gln Lys Met 275 280 285		
Lys Lys Ala Val Glu Ser Leu Met Ala Ala Asn Glu Glu Lys Asp Arg 290 295 300		
Lys Ile Glu Asp Leu Arg Gln Cys Leu Asn Arg Tyr Lys Lys Met Gln 305 310 315 320		
Asp Thr Val Val Leu Ala Gln Gly Lys Lys Gly Lys Asp Gly Glu Tyr 325 330 335		
Glu Glu Leu Leu Asn Ser Ser Ser Ile Ser Ser Leu Leu Asp Ala Gln 340 345 350		
Gly Phe Ser Asp Leu Glu Lys Ser Pro Ser Pro Thr Pro Val Met Gly 355 360 365		
Ser Pro Ser Cys Asp Pro Phe Asn Thr Ser Val Pro Glu Glu Phe His 370 375 380		
Thr Thr Ile Leu Gln Val Ser Ile Pro Ser Leu Leu Pro Ala Thr Val 385 390 395 400		
Ser Met Glu Thr Ser Glu Lys Ser Lys Leu Thr Pro Lys Pro Glu Thr 405 410 415		

Ser Phe Glu Glu Asn Asp Gly Asn Ile Ile Leu Gly Ala Thr Val Asp  
 420 425 430  
 Thr Gln Leu Arg Asp Lys Leu Leu Thr Ser Ser Leu Gln Lys Ser Ser  
 435 440 445  
 Ser Leu Gly Asn Leu Lys Lys Glu Thr Ser Asp Gly Glu Lys Glu Thr  
 450 455 460  
 Ile Gln Lys Thr Ser Glu Asp Arg Ala Pro Ala Glu Ser Arg Pro Phe  
 465 470 475 480  
 Gly Thr Leu Pro Pro Arg Pro Pro Gly Gln Asp Thr Ser Met Asp Asp  
 485 490 495  
 Asn Pro Phe Gly Thr Arg Lys Val Arg Ser Ser Phe Gly Arg Gly Phe  
 500 505 510  
 Phe Lys Ile Lys Ser Asn Lys Arg Thr Ala Ser Ala Pro Asn Leu Asp  
 515 520 525  
 Arg Lys Arg Ser Ala Ser Ala Pro Thr Leu Ala Glu Thr Glu Lys Glu  
 530 535 540  
 Thr Ala Ala His Leu Asp Leu Ala Gly Ala Ser Ser Arg Pro Lys Asp  
 545 550 555 560  
 Ser Gln Arg Asn Ser Pro Phe Gln Ile Pro Pro Pro Ser Pro Asp Ser  
 565 570 575  
 Lys Lys Lys Ser Arg Gly Ile Met Lys Leu Phe Gly Lys Leu Arg Arg  
 580 585 590  
 Ser Gln Ser Thr Thr Phe Asn Pro Asp Asp Met Ser Glu Pro Glu Phe  
 595 600 605  
 Lys Arg Gly Gly Thr Arg Ala Thr Ala Gly Pro Arg Leu Gly Trp Ser  
 610 615 620  
 Arg Asp Leu Gly Gln Ser Asn Ser Asp Leu Asp Met Pro Phe Ala Lys  
 625 630 635 640  
 Trp Thr Lys Glu Gln Val Cys Asn Trp Leu Met Glu Gln Gly Leu Gly  
 645 650 655  
 Ser Tyr Leu Asn Ser Gly Lys His Trp Ile Ala Ser Gly Gln Thr Leu  
 660 665 670  
 Leu Gln Ala Ser Gln Gln Asp Leu Glu Lys Glu Leu Gly Ile Lys His  
 675 680 685  
 Ser Leu His Arg Lys Lys Leu Gln Leu Ala Leu Gln Ala Leu Gly Ser  
 690 695 700  
 Glu Glu Glu Thr Asn His Gly Lys Leu Asp Phe Asn Trp Val Thr Arg  
 705 710 715 720  
 Trp Leu Asp Asp Ile Gly Leu Pro Gln Tyr Lys Thr Gln Phe Asp Glu  
 725 730 735



Gly Arg Val Asp Gly Arg Met Leu His Tyr Met Thr Val Asp Asp Leu  
 740 745 750  
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 Ala Ile Gln Val Leu Arg Ile Asn Asn Phe Glu Pro Asn Cys Leu Arg  
 770 775 780  
 Arg Arg Pro Ser Asp Glu Asn Thr Ile Ala Pro Ser Glu Val Gln Lys  
 785 790 795 800  
 Trp Thr Asn His Arg Val Met Glu Trp Leu Arg Ser Val Asp Leu Ala  
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 Glu Tyr Ala Pro Asn Leu Arg Gly Ser Gly Val His Gly Gly Leu Met  
 820 825 830  
 Val Leu Glu Pro Arg Phe Asn Val Glu Thr Met Ala Gln Leu Leu Asn  
 835 840 845  
 Ile Pro Pro Asn Lys Thr Leu Leu Arg Arg His Leu Ala Thr His Phe  
 850 855 860  
 Asn Leu Leu Ile Gly Ala Glu Ala Gln His Gln Lys Arg Asp Ala Met  
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 Glu Leu Pro Asp Tyr Val Leu Leu Thr Ala Thr Ala Lys Val Lys Pro  
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 Lys Lys Leu Ala Phe Ser Asn Phe Gly Asn Leu Arg Lys Lys Lys Gln  
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 915 920 925  
 Gly Ser Ala Ser Lys Lys Gly Phe Lys Pro Gly Leu Asp Met Arg Leu  
 930 935 940  
 Tyr Glu Glu Asp Asp Leu Asp Arg Leu Glu Gln Met Glu Asp Ser Glu  
 945 950 955 960  
 Gly Thr Val Arg Gln Ile Gly Ala Phe Ser Glu Gly Ile Asn Asn Leu  
 965 970 975  
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 35 40 45  
 Thr Asp Gln Asn Ser Asp Gly Tyr Cys Gln Thr Gly Thr Met Ser Arg  
 50 55 60  
 His Gln Asn Gln Asn Thr Ile Gln Glu Leu Leu Gln Asn Cys Ser Asp  
 65 70 75 80  
 Cys Leu Met Arg Ala Glu Leu Ile Val Gln Pro Glu Leu Lys Tyr Gly  
 85 90 95  
 Asp Gly Ile Gln Leu Thr Arg Ser Arg Glu Leu Asp Glu Cys Phe Ala  
 100 105 110  
 Gln Ala Asn Asp Gln Met Glu Ile Leu Asp Ser Leu Ile Arg Glu Met  
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 Arg Gln Met Gly Gln Pro Cys Asp Ala Tyr Gln Lys Arg Leu Leu Gln  
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 Leu Gln Glu Gln Met Arg Ala Leu Tyr Lys Ala Ile Ser Val Pro Arg  
 145 150 155 160  
 Val Arg Arg Ala Ser Ser Lys Gly Gly Gly Gly Tyr Thr Cys Gln Ser  
 165 170 175  
 Gly Ser Gly Trp Asp Glu Phe Thr Lys His Val Thr Ser Glu Cys Leu  
 180 185 190  
 Gly Trp Met Arg Gln Gln Arg Ala Glu Met Asp Met Val Ala Trp Gly  
 195 200 205  
 Val Asp Leu Ala Ser Val Glu Gln His Ile Asn Ser His Arg Gly Ile  
 210 215 220  
 His Asn Ser Ile Gly Asp Tyr Arg Trp Gln Leu Asp Lys Ile Lys Ala  
 225 230 235 240  
 Asp Leu Arg Glu Lys Ser Ala Ile Tyr Gln Leu Glu Glu Glu Tyr Glu  
 245 250 255  
 Asn Leu Leu Lys Ala Ser Phe Glu Arg Met Asp His Leu Arg Gln Leu  
 260 265 270  
 Gln Asn Ile Ile Gln Ala Thr Ser Arg Glu Ile Met Trp Ile Asn Asp  
 275 280 285  
 Cys Glu Glu Glu Glu Leu Leu Tyr Asp Trp Ser Asp Lys Asn Thr Asn  
 290 295 300  
 Ile Ala Gln Lys Gln Glu Ala Phe Ser Ile Arg Met Ser Gln Leu Glu  
 305 310 315 320  
 Val Lys Glu Lys Glu Leu Asn Lys Leu Lys Gln Glu Ser Asp Gln Leu  
 325 330 335

Val Leu Asn Gln His Pro Ala Ser Asp Lys Ile Glu Ala Tyr Met Asp  
 340 345 350  
 Thr Leu Gln Thr Gln Trp Ser Trp Ile Leu Gln Ile Thr Lys Cys Ile  
 355 360 365  
 Asp Val His Leu Lys Glu Asn Ala Ala Tyr Phe Gln Phe Phe Glu Glu  
 370 375 380  
 Ala Gln Ser Thr Glu Ala Tyr Leu Lys Gly Leu Gln Asp Ser Ile Arg  
 385 390 395 400  
 Lys Lys Tyr Pro Cys Asp Lys Asn Met Pro Leu Gln His Leu Leu Glu  
 405 410 415  
 Gln Ile Lys Glu Leu Glu Lys Glu Arg Glu Lys Ile Leu Glu Tyr Lys  
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 Arg Gln Val Gln Asn Leu Val Asn Lys Ser Lys Lys Ile Val Gln Leu  
 435 440 445  
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 450 455 460  
 Ala Leu Cys Asp Tyr Lys Gln Asp Gln Lys Ile Val His Lys Gly Asp  
 465 470 475 480  
 Glu Cys Ile Leu Lys Asp Asn Asn Glu Arg Ser Lys Trp Tyr Val Thr  
 485 490 495  
 Gly Pro Gly Gly Val Asp Met Leu Val Pro Ser Val Gly Leu Ile Ile  
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 Pro Pro Pro Asn Pro Leu Ala Val Asp Leu Ser Cys Lys Ile Glu Gln  
 515 520 525  
 Tyr Tyr Glu Ala Ile Leu Ala Leu Trp Asn Gln Leu Tyr Ile Asn Met  
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 Lys Ser Leu Val Ser Trp His Tyr Cys Met Ile Asp Ile Glu Lys Ile  
 545 550 555 560  
 Arg Ala Met Thr Ile Ala Lys Leu Lys Thr Met Arg Gln Glu Asp Tyr  
 565 570 575  
 Met Lys Thr Ile Ala Asp Leu Glu Leu His Tyr Gln Glu Phe Ile Arg  
 580 585 590  
 Asn Ser Gln Gly Ser Glu Met Phe Gly Asp Asp Asp Lys Arg Lys Ile  
 595 600 605  
 Gln Ser Gln Phe Thr Asp Ala Gln Lys His Tyr Gln Thr Leu Val Ile  
 610 615 620  
 Gln Leu Pro Gly Tyr Pro Gln His Gln Thr Val Thr Thr Thr Glu Ile  
 625 630 635 640  
 Thr His His Gly Thr Cys Gln Asp Val Asn His Asn Lys Val Ile Glu



Tyr Glu Leu Gln Leu Ala Ser Tyr Thr Ser Gly Leu Glu Thr Leu Leu  
 965 970 975  
 Asn Ile Pro Ile Lys Arg Thr Met Ile Gln Ser Pro Ser Gly Val Ile  
 980 985 990  
 Leu Gln Glu Ala Ala Asp Val His Ala Arg Tyr Ile Glu Leu Leu Thr  
 995 1000 1005  
 Arg Ser Gly Asp Tyr Tyr Arg Phe Leu Ser Glu Met Leu Lys Ser  
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 Leu Glu Asp Leu Lys Leu Lys Asn Thr Lys Ile Glu Val Leu Glu  
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 Glu Glu Leu Arg Leu Ala Arg Asp Ala Asn Ser Glu Asn Cys Asn  
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 Cys Ser Gln Phe Lys Ala Lys Leu Ala Ser Leu Glu Glu Leu Lys  
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 Arg Gln Ala Glu Leu Asp Gly Lys Ser Ala Lys Gln Asn Leu Asp  
 1085 1090 1095  
 Lys Cys Tyr Gly Gln Ile Lys Glu Leu Asn Glu Lys Ile Thr Arg  
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 Leu Thr Tyr Glu Ile Glu Asp Glu Lys Arg Arg Arg Lys Ser Val  
 1115 1120 1125  
 Glu Asp Arg Phe Asp Gln Gln Lys Asn Asp Tyr Asp Gln Leu Gln  
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 Lys Ala Arg Gln Cys Glu Lys Glu Asn Leu Gly Trp Gln Lys Leu  
 1145 1150 1155  
 Glu Ser Glu Lys Ala Ile Lys Glu Lys Glu Tyr Glu Ile Glu Arg  
 1160 1165 1170  
 Leu Arg Val Leu Leu Gln Glu Glu Gly Thr Arg Lys Arg Glu Tyr  
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 Glu Asn Glu Leu Ala Lys Val Arg Asn His Tyr Asn Glu Glu Met  
 1190 1195 1200  
 Ser Asn Leu Arg Asn Lys Tyr Glu Thr Glu Ile Asn Ile Thr Lys  
 1205 1210 1215  
 Thr Thr Ile Lys Glu Ile Ser Met Gln Lys Glu Asp Asp Ser Lys  
 1220 1225 1230  
 Asn Leu Arg Asn Gln Leu Asp Arg Leu Ser Arg Glu Asn Arg Asp  
 1235 1240 1245  
 Leu Lys Asp Glu Ile Val Arg Leu Asn Asp Ser Ile Leu Gln Ala  
 1250 1255 1260

Thr Glu Gln Arg Arg Arg Ala Glu Glu Asn Ala Leu Gln Gln Lys  
 1265 1270 1275  
 Ala Cys Gly Ser Glu Ile Met Gln Lys Lys Gln His Leu Glu Ile  
 1280 1285 1290  
 Glu Leu Lys Gln Val Met Gln Gln Arg Ser Glu Asp Asn Ala Arg  
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 His Lys Gln Ser Leu Glu Glu Ala Ala Lys Thr Ile Gln Asp Lys  
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 Asn Lys Glu Ile Glu Arg Leu Lys Ala Glu Phe Gln Glu Glu Ala  
 1325 1330 1335  
 Lys Arg Arg Trp Glu Tyr Glu Asn Glu Leu Ser Lys Val Arg Asn  
 1340 1345 1350  
 Asn Tyr Asp Glu Glu Ile Ile Ser Leu Lys Asn Gln Phe Glu Thr  
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 Glu Ile Asn Ile Thr Lys Thr Thr Ile His Gln Leu Thr Met Gln  
 1370 1375 1380  
 Lys Glu Glu Asp Thr Ser Gly Tyr Arg Ala Gln Ile Asp Asn Leu  
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 Thr Arg Glu Asn Arg Ser Leu Ser Glu Glu Ile Lys Arg Leu Lys  
 1400 1405 1410  
 Asn Thr Leu Thr Gln Thr Thr Glu Asn Leu Arg Arg Val Glu Glu  
 1415 1420 1425  
 Asp Ile Gln Gln Gln Lys Ala Thr Gly Ser Glu Val Ser Gln Arg  
 1430 1435 1440  
 Lys Gln Gln Leu Glu Val Glu Leu Arg Gln Val Thr Gln Met Arg  
 1445 1450 1455  
 Thr Glu Glu Ser Val Arg Tyr Lys Gln Ser Leu Asp Asp Ala Ala  
 1460 1465 1470  
 Lys Thr Ile Gln Asp Lys Asn Lys Glu Ile Glu Arg Leu Lys Gln  
 1475 1480 1485  
 Leu Ile Asp Lys Glu Thr Asn Asp Arg Lys Cys Leu Glu Asp Glu  
 1490 1495 1500  
 Asn Ala Arg Leu Gln Arg Val Gln Tyr Asp Leu Gln Lys Ala Asn  
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 Ser Ser Ala Thr Glu Thr Ile Asn Lys Leu Lys Val Gln Glu Gln  
 1520 1525 1530  
 Glu Leu Thr Arg Leu Arg Ile Asp Tyr Glu Arg Val Ser Gln Glu  
 1535 1540 1545  
 Arg Thr Val Lys Asp Gln Asp Ile Thr Arg Phe Gln Asn Ser Leu  
 1550 1555 1560

Lys Glu Leu Gln Leu Gln Lys Gln Lys Val Glu Glu Glu Leu Asn  
 1565 1570 1575  
 Arg Leu Lys Arg Thr Ala Ser Glu Asp Ser Cys Lys Arg Lys Lys  
 1580 1585 1590  
 Leu Glu Glu Glu Leu Glu Gly Met Arg Arg Ser Leu Lys Glu Gln  
 1595 1600 1605  
 Ala Ile Lys Ile Thr Asn Leu Thr Gln Gln Leu Glu Gln Ala Ser  
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 Ile Val Lys Lys Arg Ser Glu Asp Asp Leu Arg Gln Gln Arg Asp  
 1625 1630 1635  
 Val Leu Asp Gly His Leu Arg Glu Lys Gln Arg Thr Gln Glu Glu  
 1640 1645 1650  
 Leu Arg Arg Leu Ser Ser Glu Val Glu Ala Leu Arg Arg Gln Leu  
 1655 1660 1665  
 Leu Gln Glu Gln Glu Ser Val Lys Gln Ala His Leu Arg Asn Glu  
 1670 1675 1680  
 His Phe Gln Lys Ala Ile Glu Asp Lys Ser Arg Ser Leu Asn Glu  
 1685 1690 1695  
 Ser Lys Ile Glu Ile Glu Arg Leu Gln Ser Leu Thr Glu Asn Leu  
 1700 1705 1710  
 Thr Lys Glu His Leu Met Leu Glu Glu Glu Leu Arg Asn Leu Arg  
 1715 1720 1725  
 Leu Glu Tyr Asp Asp Leu Arg Arg Gly Arg Ser Glu Ala Asp Ser  
 1730 1735 1740  
 Asp Lys Asn Ala Thr Ile Leu Glu Leu Arg Ser Gln Leu Gln Ile  
 1745 1750 1755  
 Ser Asn Asn Arg Thr Leu Glu Leu Gln Gly Leu Ile Asn Asp Leu  
 1760 1765 1770  
 Gln Arg Glu Arg Glu Asn Leu Arg Gln Glu Ile Glu Lys Phe Gln  
 1775 1780 1785  
 Lys Gln Ala Leu Glu Ala Ser Asn Arg Ile Gln Glu Ser Lys Asn  
 1790 1795 1800  
 Gln Cys Thr Gln Val Val Gln Glu Arg Glu Ser Leu Leu Val Lys  
 1805 1810 1815  
 Ile Lys Val Leu Glu Gln Asp Lys Ala Arg Leu Gln Arg Leu Glu  
 1820 1825 1830  
 Asp Glu Leu Asn Arg Ala Lys Ser Thr Leu Glu Ala Glu Thr Arg  
 1835 1840 1845  
 Val Lys Gln Arg Leu Glu Cys Glu Lys Gln Gln Ile Gln Asn Asp

1850	1855	1860
Leu Asn Gln Trp Lys Thr 1865	Gln Tyr Ser Arg Lys 1870	Glu Glu Ala Ile 1875
Arg Lys Ile Glu Ser Glu 1880	Arg Glu Lys Ser Glu 1885	Arg Glu Lys Asn 1890
Ser Leu Arg Ser Glu Ile 1895	Glu Arg Leu Gln Ala 1900	Glu Ile Lys Arg 1905
Ile Glu Glu Arg Cys Arg 1910	Arg Lys Leu Glu Asp 1915	Ser Thr Arg Glu 1920
Thr Gln Ser Gln Leu Glu 1925	Thr Glu Arg Ser Arg 1930	Tyr Gln Arg Glu 1935
Ile Asp Lys Leu Arg Gln 1940	Arg Pro Tyr Gly Ser 1945	His Arg Glu Thr 1950
Gln Thr Glu Cys Glu Trp 1955	Thr Val Asp Thr Ser 1960	Lys Leu Val Phe 1965
Asp Gly Leu Arg Lys Lys 1970	Val Thr Ala Met Gln 1975	Leu Tyr Glu Cys 1980
Gln Leu Ile Asp Lys Thr 1985	Thr Leu Asp Lys Leu 1990	Leu Lys Gly Lys 1995
Lys Ser Val Glu Glu Val 2000	Ala Ser Glu Ile Gln 2005	Pro Phe Leu Arg 2010
Gly Ala Gly Ser Ile Ala 2015	Gly Ala Ser Ala Ser 2020	Pro Lys Glu Lys 2025
Tyr Ser Leu Val Glu Ala 2030	Lys Arg Lys Lys Leu 2035	Ile Ser Pro Glu 2040
Ser Thr Val Met Leu Leu 2045	Glu Ala Gln Ala Ala 2050	Thr Gly Gly Ile 2055
Ile Asp Pro His Arg Asn 2060	Glu Lys Leu Thr Val 2065	Asp Ser Ala Ile 2070
Ala Arg Asp Leu Ile Asp 2075	Phe Asp Asp Arg Gln 2080	Gln Ile Tyr Ala 2085
Ala Glu Lys Ala Ile Thr 2090	Gly Phe Asp Asp Pro 2095	Phe Ser Gly Lys 2100
Thr Val Ser Val Ser Glu 2105	Ala Ile Lys Lys Asn 2110	Leu Ile Asp Arg 2115
Glu Thr Gly Met Arg Leu 2120	Leu Glu Ala Gln Ile 2125	Ala Ser Gly Gly 2130
Val Val Asp Pro Val Asn 2135	Ser Val Phe Leu Pro 2140	Lys Asp Val Ala 2145



Leu Ala Arg Gly Leu Ile Asp Arg Asp Leu Tyr Arg Ser Leu Asn  
 2150 2155 2160  
 Asp Pro Arg Asp Ser Gln Lys Asn Phe Val Asp Pro Val Thr Lys  
 2165 2170 2175  
 Lys Lys Val Ser Tyr Val Gln Leu Lys Glu Arg Cys Arg Ile Glu  
 2180 2185 2190  
 Pro His Thr Gly Leu Leu Leu Leu Ser Val Gln Lys Arg Ser Met  
 2195 2200 2205  
 Ser Phe Gln Gly Ile Arg Gln Pro Val Thr Val Thr Glu Leu Val  
 2210 2215 2220  
 Asp Ser Gly Ile Leu Arg Pro Ser Thr Val Asn Glu Leu Glu Ser  
 2225 2230 2235  
 Gly Gln Ile Ser Tyr Asp Glu Val Gly Glu Arg Ile Lys Asp Phe  
 2240 2245 2250  
 Leu Gln Gly Ser Ser Cys Ile Ala Gly Ile Tyr Asn Glu Thr Thr  
 2255 2260 2265  
 Lys Gln Lys Leu Gly Ile Tyr Glu Ala Met Lys Ile Gly Leu Val  
 2270 2275 2280  
 Arg Pro Gly Thr Ala Leu Glu Leu Leu Glu Ala Gln Ala Ala Thr  
 2285 2290 2295  
 Gly Phe Ile Val Asp Pro Val Ser Asn Leu Arg Leu Pro Val Glu  
 2300 2305 2310  
 Glu Ala Tyr Lys Arg Gly Leu Val Gly Ile Glu Phe Lys Glu Lys  
 2315 2320 2325  
 Leu Leu Ser Ala Glu Arg Ala Val Thr Gly Tyr Asn Asp Pro Glu  
 2330 2335 2340  
 Thr Gly Asn Ile Ile Ser Leu Phe Gln Ala Met Asn Lys Glu Leu  
 2345 2350 2355  
 Ile Glu Lys Gly His Gly Ile Arg Leu Leu Glu Ala Gln Ile Ala  
 2360 2365 2370  
 Thr Gly Gly Ile Ile Asp Pro Lys Glu Ser His Arg Leu Pro Val  
 2375 2380 2385  
 Asp Ile Ala Tyr Lys Arg Gly Tyr Phe Asn Glu Glu Leu Ser Glu  
 2390 2395 2400  
 Ile Leu Ser Asp Pro Ser Asp Asp Thr Lys Gly Phe Phe Asp Pro  
 2405 2410 2415  
 Asn Thr Glu Glu Asn Leu Thr Tyr Leu Gln Leu Lys Glu Arg Cys  
 2420 2425 2430  
 Ile Lys Asp Glu Glu Thr Gly Leu Cys Leu Leu Pro Leu Lys Glu  
 2435 2440 2445

Lys Lys Lys Gln Val Gln Thr Ser Gln Lys Asn Thr Leu Arg Lys  
 2450 2455 2460  
 Arg Arg Val Val Ile Val Asp Pro Glu Thr Asn Lys Glu Met Ser  
 2465 2470 2475  
 Val Gln Glu Ala Tyr Lys Lys Gly Leu Ile Asp Tyr Glu Thr Phe  
 2480 2485 2490  
 Lys Glu Leu Cys Glu Gln Glu Cys Glu Trp Glu Glu Ile Thr Ile  
 2495 2500 2505  
 Thr Gly Ser Asp Gly Ser Thr Arg Val Val Leu Val Asp Arg Lys  
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 Thr Gly Ser Gln Tyr Asp Ile Gln Asp Ala Ile Asp Lys Gly Leu  
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 Val Asp Arg Lys Phe Phe Asp Gln Tyr Arg Ser Gly Ser Leu Ser  
 2540 2545 2550  
 Leu Thr Gln Phe Ala Asp Met Ile Ser Leu Lys Asn Gly Val Gly  
 2555 2560 2565  
 Thr Ser Ser Ser Met Gly Ser Gly Val Ser Asp Asp Val Phe Ser  
 2570 2575 2580  
 Ser Ser Arg His Glu Ser Val Ser Lys Ile Ser Thr Ile Ser Ser  
 2585 2590 2595  
 Val Arg Asn Leu Thr Ile Arg Ser Ser Ser Phe Ser Asp Thr Leu  
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 Glu Glu Ser Ser Pro Ile Ala Ala Ile Phe Asp Thr Glu Asn Leu  
 2615 2620 2625  
 Glu Lys Ile Ser Ile Thr Glu Gly Ile Glu Arg Gly Ile Val Asp  
 2630 2635 2640  
 Ser Ile Thr Gly Gln Arg Leu Leu Glu Ala Gln Ala Cys Thr Gly  
 2645 2650 2655  
 Gly Ile Ile His Pro Thr Thr Gly Gln Lys Leu Ser Leu Gln Asp  
 2660 2665 2670  
 Ala Val Ser Gln Gly Val Ile Asp Gln Asp Met Ala Thr Ser Val  
 2675 2680 2685  
 Lys Pro Ala Gln Lys Ala Phe Ile Gly Phe Glu Gly Val Lys Gly  
 2690 2695 2700  
 Lys Lys Lys Met Ser Ala Ala Glu Ala Val Lys Glu Lys Trp Leu  
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 Pro Tyr Glu Ala Gly Gln Arg Phe Leu Glu Phe Gln Tyr Leu Thr  
 2720 2725 2730  
 Gly Gly Leu Val Asp Pro Glu Val His Gly Arg Ile Ser Thr Glu  
 2735 2740 2745

Glu Ala Ile Arg Lys Gly Phe Ile Asp Gly Arg Ala Ala Gln Arg  
 2750 2755 2760  
 Leu Gln Asp Thr Ser Ser Tyr Ala Lys Ile Leu Thr Cys Pro Lys  
 2765 2770 2775  
 Thr Lys Leu Lys Ile Ser Tyr Lys Asp Ala Ile Asn Arg Ser Met  
 2780 2785 2790  
 Val Glu Asp Ile Thr Gly Leu Arg Leu Leu Glu Ala Ala Ser Val  
 2795 2800 2805  
 Ser Ser Lys Gly Leu Pro Ser Pro Tyr Asn Met Ser Ser Ala Pro  
 2810 2815 2820  
 Gly Ser Arg Ser Gly Ser Arg Ser Gly Ser Arg Ser Gly Ser Arg  
 2825 2830 2835  
 Ser Gly Ser Arg Ser Gly Ser Arg Arg Gly Ser Phe Asp Ala Thr  
 2840 2845 2850  
 Gly Asn Ser Ser Tyr Ser Tyr Ser Tyr Ser Phe Ser Ser Ser Ser  
 2855 2860 2865  
 Ile Gly His  
 2870

<210> 113  
 <211> 381  
 <212> PRT  
 <213> Homo sapiens

<400> 113

Met Trp Arg Leu Met Ser Arg Phe Asn Ala Phe Lys Arg Thr Asn Thr  
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 Ile Leu His His Leu Arg Met Ser Lys His Thr Asp Ala Ala Glu Glu  
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 Val Leu Leu Glu Lys Lys Gly Cys Ala Gly Val Ile Thr Leu Asn Arg  
 35 40 45  
 Pro Lys Phe Leu Asn Ala Leu Thr Leu Asn Met Ile Arg Gln Ile Tyr  
 50 55 60  
 Pro Gln Leu Lys Lys Trp Glu Gln Asp Pro Glu Thr Phe Val Ile Ile  
 65 70 75 80  
 Ile Lys Gly Ala Gly Gly Lys Ala Phe Cys Ala Gly Gly Asp Ile Arg  
 85 90 95  
 Val Ile Ser Glu Ala Glu Lys Ala Lys Gln Lys Ile Ala Pro Val Phe  
 100 105 110  
 Phe Arg Glu Glu Tyr Met Leu Asn Asn Ala Val Gly Ser Cys Gln Lys  
 115 120 125  
 Pro Tyr Val Ala Leu Ile His Gly Ile Thr Met Gly Gly Gly Val Gly  
 130 135 140

Leu Ser Val His Gly Gln Phe Arg Val Ala Thr Glu Lys Cys Leu Phe  
145 150 155 160

Ala Met Pro Glu Thr Ala Ile Gly Leu Phe Pro Asp Val Gly Gly Gly  
165 170 175

Tyr Phe Phe Ala Thr Thr Pro Arg Lys Thr Trp Leu Leu Pro Cys Ile  
180 185 190

Asn Gly Phe Arg Leu Lys Gly Arg Asp Val Tyr Arg Ala Gly Ile Ala  
195 200 205

Thr His Phe Val Asp Ser Glu Lys Leu Ala Met Leu Glu Glu Asp Leu  
210 215 220

Leu Ala Leu Lys Ser Pro Ser Lys Glu Asn Ile Ala Ser Val Leu Glu  
225 230 235 240

Asn Tyr His Thr Glu Ser Lys Ile Asp Arg Asp Lys Ser Phe Ile Leu  
245 250 255

Glu Glu His Met Asp Lys Ile Asn Ser Cys Phe Ser Ala Asn Thr Val  
260 265 270

Glu Glu Ile Ile Glu Asn Leu Gln Gln Asp Gly Ser Ser Phe Ala Leu  
275 280 285

Glu Gln Leu Lys Val Ile Asn Lys Met Ser Pro Thr Ser Leu Lys Ile  
290 295 300

Thr Leu Arg Gln Leu Met Glu Gly Ser Ser Lys Thr Leu Gln Glu Val  
305 310 315 320

Leu Thr Met Glu Tyr Arg Leu Ser Gln Ala Cys Met Arg Gly His Asp  
325 330 335

Phe His Glu Gly Val Arg Ala Val Leu Ile Asp Lys Asp Gln Ser Pro  
340 345 350

Lys Trp Lys Pro Ala Asp Leu Lys Glu Val Thr Glu Glu Asp Leu Asn  
355 360 365

Asn His Phe Lys Ser Leu Gly Ser Ser Asp Leu Lys Phe  
370 375 380

<210> 114  
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<400> 114

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Asn Thr Ser Pro Phe Lys Val Pro Gly Phe Phe Ser Lys Arg Leu Lys  
35 40 45

Gly Ser Ile Lys Arg Thr Lys Ser Gln Ser Lys Leu Asp Arg Asn Thr  
 50 55 60  
 Ser Phe Arg Leu Pro Ser Leu Arg Ser Thr Asp Asp Arg Ser Arg Gly  
 65 70 75 80  
 Leu Pro Lys Leu Lys Glu Ser Arg Ser His Glu Ser Leu Leu Ser Pro  
 85 90 95  
 Cys Ser Thr Val Glu Cys Leu Asp Leu Gly Arg Gly Glu Pro Val Ser  
 100 105 110  
 Val Lys Pro Leu His Ser Ser Ile Leu Gly Gln Asp Phe Cys Phe Glu  
 115 120 125  
 Val Thr Tyr Leu Ser Gly Ser Lys Cys Phe Ser Cys Asn Ser Ala Ser  
 130 135 140  
 Glu Arg Asp Lys Trp Met Glu Asn Leu Arg Arg Thr Val Gln Pro Asn  
 145 150 155 160  
 Lys Asp Asn Cys Arg Arg Ala Glu Asn Val Leu Arg Leu Trp Ile Ile  
 165 170 175  
 Glu Ala Lys Asp Leu Ala Pro Lys Lys Lys Tyr Phe Cys Glu Leu Cys  
 180 185 190  
 Leu Asp Asp Thr Leu Phe Ala Arg Thr Thr Ser Lys Thr Lys Ala Asp  
 195 200 205  
 Asn Ile Phe Trp Gly Glu His Phe Glu Phe Phe Ser Leu Pro Pro Leu  
 210 215 220  
 His Ser Ile Thr Val His Ile Tyr Lys Asp Val Glu Lys Lys Lys Lys  
 225 230 235 240  
 Lys Asp Lys Asn Asn Tyr Val Gly Leu Val Asn Ile Pro Thr Ala Ser  
 245 250 255  
 Val Thr Gly Arg Gln Phe Val Glu Lys Trp Tyr Pro Val Ser Thr Pro  
 260 265 270  
 Thr Pro Asn Lys Gly Lys Thr Gly Gly Pro Ser Ile Arg Ile Lys Ser  
 275 280 285  
 Arg Phe Gln Thr Ile Thr Ile Leu Pro Met Glu Gln Tyr Lys Glu Phe  
 290 295 300  
 Ala Glu Phe Val Thr Ser Asn Tyr Thr Met Leu Cys Ser Val Leu Glu  
 305 310 315 320  
 Pro Val Ile Ser Val Arg Asn Lys Glu Glu Leu Ala Cys Ala Leu Val  
 325 330 335  
 His Ile Leu Gln Ser Thr Gly Arg Ala Lys Asp Phe Leu Thr Asp Leu  
 340 345 350  
 Val Met Ser Glu Val Asp Arg Cys Gly Glu His Asp Val Leu Ile Phe

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355          360          365
Arg Glu Asn Thr Ile Ala Thr Lys Ser Ile Glu Glu Tyr Leu Lys Leu
370          375          380

Val Gly Gln Gln Tyr Leu His Asp Ala Leu Gly Glu Phe Ile Lys Ala
385          390          395          400

Leu Tyr Glu Ser Asp Glu Asn Cys Glu Val Asp Pro Ser Lys Cys Ser
405          410          415

Ser Ser Glu Leu Ile Asp His Gln Ser Asn Leu Lys Met Cys Cys Glu
420          425          430

Leu Ala Phe Cys Lys Ile Ile Asn Ser Tyr Cys Val Phe Pro Arg Glu
435          440          445

Leu Lys Glu Val Phe Ala Ser Trp Lys Gln Gln Cys Leu Asn Arg Gly
450          455          460

Lys Gln Asp Ile Ser Glu Arg Leu Ile Ser Ala Ser Leu Phe Leu Arg
465          470          475          480

Phe Leu Cys Pro Ala Ile Met Ser Pro Ser Leu Phe Asn Leu Met Gln
485          490          495

Glu Tyr Pro Asp Asp Arg Thr Ser Arg Thr Leu Thr Leu Ile Ala Lys
500          505          510

Val Ile Gln Asn Leu Ala Asn Phe Ala Lys Phe Gly Asn Lys Glu Glu
515          520          525

Tyr Met Ala Phe Met Asn Asp Phe Leu Glu His Glu Trp Gly Gly Met
530          535          540

Lys Arg Phe Leu Leu Glu Ile Ser Asn Pro Asp Thr Ile Ser Asn Thr
545          550          555          560

Pro Gly Phe Asp Gly Tyr Ile Asp Leu Gly Arg Glu Leu Ser Val Leu
565          570          575

His Ser Leu Leu Trp Glu Val Val Ser Gln Leu Asp Lys Gly Glu Asn
580          585          590

Ser Phe Leu Gln Ala Thr Val Ala Lys Leu Gly Pro Leu Pro Arg Val
595          600          605

Leu Ala Asp Ile Thr Lys Ser Leu Thr Asn Pro Thr Pro Ile Gln Gln
610          615          620

Gln Leu Arg Arg Phe Thr Glu His Asn Ser Ser Pro Asn Val Ser Gly
625          630          635          640

Ser Leu Ser Ser Gly Leu Gln Lys Ile Phe Glu Asp Pro Thr Asp Ser
645          650          655

Asp Leu His Lys Leu Lys Ser Pro Ser Gln Asp Asn Thr Asp Ser Tyr
660          665          670

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Phe Arg Gly Lys Thr Leu Leu Leu Val Gln Gln Ala Ser Ser Gln Ser  
 675 680 685  
 Met Thr Tyr Ser Glu Lys Asp Glu Arg Glu Ser Ser Leu Pro Asn Gly  
 690 695 700  
 Arg Ser Val Ser Leu Met Asp Leu Gln Asp Thr His Ala Ala Gln Val  
 705 710 715 720  
 Glu His Ala Ser Val Met Leu Asp Val Pro Ile Arg Leu Thr Gly Ser  
 725 730 735  
 Gln Leu Ser Ile Thr Gln Val Ala Ser Ile Lys Gln Leu Arg Glu Thr  
 740 745 750  
 Gln Ser Thr Pro Gln Ser Ala Pro Gln Val Arg Arg Pro Leu His Pro  
 755 760 765  
 Ala Leu Asn Gln Pro Gly Gly Leu Gln Pro Leu Ser Phe Gln Asn Pro  
 770 775 780  
 Val Tyr His Leu Asn Asn Pro Ile Pro Ala Met Pro Lys Ala Ser Ile  
 785 790 795 800  
 Asp Ser Ser Leu Glu Asn Leu Ser Thr Ala Ser Ser Arg Ser Gln Ser  
 805 810 815  
 Asn Ser Glu Asp Phe Lys Leu Ser Gly Pro Ser Asn Ser Ser Met Glu  
 820 825 830  
 Asp Phe Thr Lys Arg Ser Thr Gln Ser Glu Asp Phe Ser Arg Arg His  
 835 840 845  
 Thr Val Pro Asp Arg His Ile Pro Leu Ala Leu Pro Arg Gln Asn Ser  
 850 855 860  
 Thr Gly Gln Ala Gln Ile Arg Lys Val Asp Gln Gly Gly Leu Gly Ala  
 865 870 875 880  
 Arg Ala Lys Ala Pro Pro Ser Leu Pro His Ser Ala Ser Leu Arg Ser  
 885 890 895  
 Thr Gly Ser Met Ser Val Val Ser Ala Ala Leu Val Ala Glu Pro Val  
 900 905 910  
 Gln Asn Gly Ser Arg Ser Arg Gln Gln Ser Ser Ser Ser Arg Glu Ser  
 915 920 925  
 Pro Val Pro Lys Val Arg Ala Ile Gln Arg Gln Gln Thr Gln Gln Val  
 930 935 940  
 Gln Ser Pro Val Asp Ser Ala Thr Met Ser Pro Val Glu Arg Thr Ala  
 945 950 955 960  
 Ala Trp Val Leu Asn Asn Gly Gln Tyr Glu Glu Asp Val Glu Glu Thr  
 965 970 975  
 Glu Gln Asn Leu Asp Glu Ala Lys His Ala Glu Lys Tyr Glu Gln Glu  
 980 985 990

Ile Thr Lys Leu Lys Glu Arg Leu Arg Val Ser Ser Arg Arg Leu Glu  
995 1000 1005

Glu Tyr Glu Arg Arg Leu Leu Val Gln Glu Gln Gln Met Gln Lys  
1010 1015 1020

Leu Leu Leu Glu Tyr Lys Ala Arg Leu Glu Asp Ser Glu Glu Arg  
1025 1030 1035

Leu Arg Arg Gln Gln Glu Glu Lys Asp Ser Gln Met Lys Ser Ile  
1040 1045 1050

Ile Ser Arg Leu Met Ala Val Glu Glu Glu Leu Lys Lys Asp His  
1055 1060 1065

Ala Glu Met Gln Ala Val Ile Asp Ala Lys Gln Lys Ile Ile Asp  
1070 1075 1080

Ala Gln Glu Lys Arg Ile Val Ser Leu Asp Ser Ala Asn Thr Arg  
1085 1090 1095

Leu Met Ser Ala Leu Thr Gln Val Lys Glu Arg Tyr Ser Met Gln  
1100 1105 1110

Val Arg Asn Gly Ile Ser Pro Thr Asn Pro Thr Lys Leu Ser Ile  
1115 1120 1125

Thr Glu Asn Gly Glu Phe Lys Asn Ser Ser Cys  
1130 1135

<210> 115  
<211> 165  
<212> PRT  
<213> Homo sapiens

<400> 115

Met Thr Leu Glu Glu Phe Ser Ala Gly Glu Gln Lys Thr Glu Arg Met  
1 5 10 15

Asp Lys Val Gly Asp Ala Leu Glu Glu Val Leu Ser Lys Ala Leu Ser  
20 25 30

Gln Arg Thr Ile Thr Val Gly Val Tyr Glu Ala Ala Lys Leu Leu Asn  
35 40 45

Val Asp Pro Asp Asn Val Val Leu Cys Leu Leu Ala Ala Asp Glu Asp  
50 55 60

Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr Leu Ile Gln Ala  
65 70 75 80

Phe Cys Cys Glu Asn Asp Ile Asn Ile Leu Arg Val Ser Asn Pro Gly  
85 90 95

Arg Leu Ala Glu Leu Leu Leu Leu Glu Thr Asp Ala Gly Pro Ala Ala  
100 105 110

Ser Glu Gly Ala Glu Gln Pro Pro Asp Leu His Cys Val Leu Val Thr  
115 120 125



Asn Pro His Ser Ser Gln Trp Lys Asp Pro Ala Leu Ser Gln Leu Ile  
 130 135 140

Cys Phe Cys Arg Glu Ser Arg Tyr Met Asp Gln Trp Val Pro Val Ile  
 145 150 155 160

Asn Leu Pro Glu Arg  
 165

<210> 116  
 <211> 1163  
 <212> PRT  
 <213> Homo sapiens

<400> 116

Met Thr Arg Thr Arg Ala Ala Leu Leu Leu Phe Thr Ala Leu Ala Thr  
 1 5 10 15

Ser Leu Gly Phe Asn Leu Asp Thr Glu Glu Leu Thr Ala Phe Arg Val  
 20 25 30

Asp Ser Ala Gly Phe Gly Asp Ser Val Val Gln Tyr Ala Asn Ser Trp  
 35 40 45

Val Val Val Gly Ala Pro Gln Lys Ile Thr Ala Ala Asn Gln Thr Gly  
 50 55 60

Gly Leu Tyr Gln Cys Gly Tyr Ser Thr Gly Ala Cys Glu Pro Ile Gly  
 65 70 75 80

Leu Gln Val Pro Pro Glu Ala Val Asn Met Ser Leu Gly Leu Ser Leu  
 85 90 95

Ala Ser Thr Thr Ser Pro Ser Gln Leu Leu Ala Cys Gly Pro Thr Val  
 100 105 110

His His Glu Cys Gly Arg Asn Met Tyr Leu Thr Gly Leu Cys Phe Leu  
 115 120 125

Leu Gly Pro Thr Gln Leu Thr Gln Arg Leu Pro Val Ser Arg Gln Glu  
 130 135 140

Cys Pro Arg Gln Glu Gln Asp Ile Val Phe Leu Ile Asp Gly Ser Gly  
 145 150 155 160

Ser Ile Ser Ser Arg Asn Phe Ala Thr Met Met Asn Phe Val Arg Ala  
 165 170 175

Val Ile Ser Gln Phe Gln Arg Pro Ser Thr Gln Phe Ser Leu Met Gln  
 180 185 190

Phe Ser Asn Lys Phe Gln Thr His Leu Thr Phe Glu Glu Phe Arg Arg  
 195 200 205

Thr Ser Asn Pro Leu Ser Leu Leu Ala Ser Val His Gln Leu Gln Gly  
 210 215 220

Phe Thr Tyr Thr Ala Thr Ala Ile Gln Asn Val Val His Arg Leu Phe  
 225 230 235 240

His Ala Ser Tyr Gly Ala Arg Arg Asp Ala Thr Lys Ile Leu Ile Val  
 245 250 255  
 Ile Thr Asp Gly Lys Lys Glu Gly Asp Thr Leu Asp Tyr Lys Asp Val  
 260 265 270  
 Ile Pro Met Ala Asp Ala Ala Gly Ile Ile Arg Tyr Ala Ile Gly Val  
 275 280 285  
 Gly Leu Ala Phe Gln Asn Arg Asn Ser Trp Lys Glu Leu Asn Asp Ile  
 290 295 300  
 Ala Ser Lys Pro Ser Gln Glu His Ile Phe Lys Val Glu Asp Phe Asp  
 305 310 315 320  
 Ala Leu Lys Asp Ile Gln Thr Gln Leu Arg Glu Lys Ile Phe Pro Ile  
 325 330 335  
 Glu Gly Thr Glu Thr Thr Ser Ser Ser Ser Phe Glu Leu Glu Met Ala  
 340 345 350  
 Gln Glu Gly Phe Ser Ala Val Phe Thr Pro Asp Gly Pro Val Leu Gly  
 355 360 365  
 Ala Val Gly Ser Phe Thr Trp Ser Gly Gly Ala Phe Leu Tyr Pro Pro  
 370 375 380  
 Asn Met Ser Pro Thr Phe Ile Asn Met Ser Gln Glu Asn Val Asp Met  
 385 390 395 400  
 Arg Asp Ser Tyr Leu Gly Tyr Ser Thr Glu Leu Ala Leu Trp Lys Gly  
 405 410 415  
 Val Gln Ser Leu Val Leu Gly Ala Pro Arg Tyr Gln His Thr Gly Lys  
 420 425 430  
 Ala Val Ile Phe Thr Gln Val Ser Arg Gln Trp Arg Met Lys Ala Glu  
 435 440 445  
 Val Thr Gly Thr Gln Ile Gly Ser Tyr Phe Gly Pro Ser Leu Cys Ser  
 450 455 460  
 Val Asp Val Asp Ser Asp Gly Ser Thr Asp Leu Val Leu Ile Gly Pro  
 465 470 475 480  
 Pro His Tyr Tyr Glu Gln Thr Arg Gly Ala Gln Val Ser Val Cys Pro  
 485 490 495  
 Leu Pro Arg Gly Trp Arg Arg Trp Trp Cys Asp Ala Val Leu Tyr Gly  
 500 505 510  
 Glu Gln Gly His Pro Trp Gly Arg Phe Gly Ala Ala Leu Thr Val Leu  
 515 520 525  
 Gly Asp Val Asn Gly Asp Lys Leu Thr Asp Val Val Ile Gly Ala Pro  
 530 535 540  
 Gly Glu Glu Glu Asn Arg Gly Ala Val Tyr Leu Phe His Gly Val Leu  
 545 550 555 560

Gly Pro Ser Ile Ser Pro Ser His Ser Gln Arg Ile Ala Gly Ser Gln  
 565 570 575  
 Leu Ser Ser Arg Leu Gln Tyr Phe Gly Gln Ala Leu Ser Gly Gly Gln  
 580 585 590  
 Asp Leu Thr Gln Asp Gly Leu Val Asp Leu Ala Val Gly Ala Arg Gly  
 595 600 605  
 Gln Val Leu Leu Leu Arg Thr Arg Pro Val Leu Trp Val Gly Val Ser  
 610 615 620  
 Met Gln Phe Ile Pro Ala Glu Ile Pro Arg Ser Ala Phe Glu Cys Arg  
 625 630 635 640  
 Glu Gln Val Val Ser Glu Gln Thr Leu Val Gln Ser Asn Ile Cys Leu  
 645 650 655  
 Tyr Ile Asp Lys Arg Ser Lys Asn Leu Leu Gly Ser Arg Asp Leu Gln  
 660 665 670  
 Ser Ser Val Thr Leu Asp Leu Ala Leu Asp Pro Gly Arg Leu Ser Pro  
 675 680 685  
 Arg Ala Thr Phe Gln Glu Thr Lys Asn Arg Ser Leu Ser Arg Val Arg  
 690 695 700  
 Val Leu Gly Leu Lys Ala His Cys Glu Asn Phe Asn Leu Leu Leu Pro  
 705 710 715 720  
 Ser Cys Val Glu Asp Ser Val Thr Pro Ile Thr Leu Arg Leu Asn Phe  
 725 730 735  
 Thr Leu Val Gly Lys Pro Leu Leu Ala Phe Arg Asn Leu Arg Pro Met  
 740 745 750  
 Leu Ala Ala Asp Ala Gln Arg Tyr Phe Thr Ala Ser Leu Pro Phe Glu  
 755 760 765  
 Lys Asn Cys Gly Ala Asp His Ile Cys Gln Asp Asn Leu Gly Ile Ser  
 770 775 780  
 Phe Ser Phe Pro Gly Leu Lys Ser Leu Leu Val Gly Ser Asn Leu Glu  
 785 790 795 800  
 Leu Asn Ala Glu Val Met Val Trp Asn Asp Gly Glu Asp Ser Tyr Gly  
 805 810 815  
 Thr Thr Ile Thr Phe Ser His Pro Ala Gly Leu Ser Tyr Arg Tyr Val  
 820 825 830  
 Ala Glu Gly Gln Lys Gln Gly Gln Leu Arg Ser Leu His Leu Thr Cys  
 835 840 845  
 Asp Ser Ala Pro Val Gly Ser Gln Gly Thr Trp Ser Thr Ser Cys Arg  
 850 855 860  
 Ile Asn His Leu Ile Phe Arg Gly Gly Ala Gln Ile Thr Phe Leu Ala

865		870		875		880
Thr Phe Asp Val Ser Pro Lys Ala Val Leu Gly Asp Arg Leu Leu Leu	885		890		895	
Thr Ala Asn Val Ser Ser Glu Asn Asn Thr Pro Arg Thr Ser Lys Thr	900		905		910	
Thr Phe Gln Leu Glu Leu Pro Val Lys Tyr Ala Val Tyr Thr Val Val	915		920		925	
Ser Ser His Glu Gln Phe Thr Lys Tyr Leu Asn Phe Ser Glu Ser Glu	930		935		940	
Glu Lys Glu Ser His Val Ala Met His Arg Tyr Gln Val Asn Asn Leu	945		950		955	960
Gly Gln Arg Asp Leu Pro Val Ser Ile Asn Phe Trp Val Pro Val Glu	965		970		975	
Leu Asn Gln Glu Ala Val Trp Met Asp Val Glu Val Ser Leu Pro Gln	980		985		990	
Asn Pro Ser Leu Arg Cys Ser Ser Glu Lys Ile Ala Gly Pro Ala Ser	995		1000		1005	
Asp Phe Leu Ala His Ile Gln Lys Asn Pro Val Leu Asp Cys Ser	1010		1015		1020	
Ile Ala Gly Cys Leu Arg Phe Arg Cys Asp Val Pro Ser Phe Ser	1025		1030		1035	
Val Gln Glu Glu Leu Asp Phe Thr Leu Lys Gly Asn Leu Ser Phe	1040		1045		1050	
Gly Trp Val Arg Gln Ile Leu Gln Lys Lys Val Ser Val Val Ser	1055		1060		1065	
Val Ala Glu Ile Thr Phe Asp Thr Ser Val Tyr Ser Gln Leu Pro	1070		1075		1080	
Gly Gln Glu Ala Phe Met Arg Ala Gln Thr Thr Thr Val Leu Glu	1085		1090		1095	
Lys Tyr Lys Val His Asn Pro Thr Pro Leu Ile Val Gly Ser Ser	1100		1105		1110	
Ile Gly Gly Leu Leu Leu Leu Ala Leu Ile Thr Ala Val Leu Tyr	1115		1120		1125	
Lys Val Gly Phe Phe Lys Arg Gln Tyr Lys Glu Met Met Glu Glu	1130		1135		1140	
Ala Asn Gly Gln Ile Ala Pro Glu Asn Gly Thr Gln Thr Pro Ser	1145		1150		1155	
Pro Pro Ser Glu Lys	1160					

<210> 117  
 <211> 335  
 <212> PRT  
 <213> Homo sapiens

<400> 117

Met Leu Gly Ile Trp Thr Leu Leu Pro Leu Val Leu Thr Ser Val Ala  
 1 5 10 15

Arg Leu Ser Ser Lys Ser Val Asn Ala Gln Val Thr Asp Ile Asn Ser  
 20 25 30

Lys Gly Leu Glu Leu Arg Lys Thr Val Thr Thr Val Glu Thr Gln Asn  
 35 40 45

Leu Glu Gly Leu His His Asp Gly Gln Phe Cys His Lys Pro Cys Pro  
 50 55 60

Pro Gly Glu Arg Lys Ala Arg Asp Cys Thr Val Asn Gly Asp Glu Pro  
 65 70 75 80

Asp Cys Val Pro Cys Gln Glu Gly Lys Glu Tyr Thr Asp Lys Ala His  
 85 90 95

Phe Ser Ser Lys Cys Arg Arg Cys Arg Leu Cys Asp Glu Gly His Gly  
 100 105 110

Leu Glu Val Glu Ile Asn Cys Thr Arg Thr Gln Asn Thr Lys Cys Arg  
 115 120 125

Cys Lys Pro Asn Phe Phe Cys Asn Ser Thr Val Cys Glu His Cys Asp  
 130 135 140

Pro Cys Thr Lys Cys Glu His Gly Ile Ile Lys Glu Cys Thr Leu Thr  
 145 150 155 160

Ser Asn Thr Lys Cys Lys Glu Glu Gly Ser Arg Ser Asn Leu Gly Trp  
 165 170 175

Leu Cys Leu Leu Leu Leu Pro Ile Pro Leu Ile Val Trp Val Lys Arg  
 180 185 190

Lys Glu Val Gln Lys Thr Cys Arg Lys His Arg Lys Glu Asn Gln Gly  
 195 200 205

Ser His Glu Ser Pro Thr Leu Asn Pro Glu Thr Val Ala Ile Asn Leu  
 210 215 220

Ser Asp Val Asp Leu Ser Lys Tyr Ile Thr Thr Ile Ala Gly Val Met  
 225 230 235 240

Thr Leu Ser Gln Val Lys Gly Phe Val Arg Lys Asn Gly Val Asn Glu  
 245 250 255

Ala Lys Ile Asp Glu Ile Lys Asn Asp Asn Val Gln Asp Thr Ala Glu  
 260 265 270

Gln Lys Val Gln Leu Leu Arg Asn Trp His Gln Leu His Gly Lys Lys  
 275 280 285

Glu Ala Tyr Asp Thr Leu Ile Lys Asp Leu Lys Lys Ala Asn Leu Cys  
290 295 300

Thr Leu Ala Glu Lys Ile Gln Thr Ile Ile Leu Lys Asp Ile Thr Ser  
305 310 315 320

Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val  
325 330 335

<210> 118  
<211> 1251  
<212> PRT  
<213> Homo sapiens

<400> 118

Met Glu Leu Ser Asp Val Arg Cys Leu Thr Gly Ser Glu Glu Leu Tyr  
1 5 10 15

Thr Ile His Pro Thr Pro Pro Ala Gly Asp Gly Arg Ser Ala Ser Arg  
20 25 30

Pro Gln Arg Leu Leu Trp Gln Thr Ala Val Arg His Ile Thr Glu Gln  
35 40 45

Arg Phe Ile His Gly His Arg Gly Gly Ser Gly Ser Gly Ser Gly Gly  
50 55 60

Ser Gly Lys Ala Ser Asp Pro Ala Gly Gly Gly Pro Asn His His Ala  
65 70 75 80

Pro Gln Leu Ser Gly Asp Ser Ala Leu Pro Leu Tyr Ser Leu Gly Pro  
85 90 95

Gly Glu Arg Ala His Ser Thr Cys Gly Thr Lys Val Phe Pro Glu Arg  
100 105 110

Ser Gly Ser Gly Ser Ala Ser Gly Ser Gly Gly Gly Gly Asp Leu Gly  
115 120 125

Phe Leu His Leu Asp Cys Ala Pro Ser Asn Ser Asp Phe Phe Leu Asn  
130 135 140

Gly Gly Tyr Ser Tyr Arg Gly Val Ile Phe Pro Thr Leu Arg Asn Ser  
145 150 155 160

Phe Lys Ser Arg Asp Leu Glu Arg Leu Tyr Gln Arg Tyr Phe Leu Gly  
165 170 175

Gln Arg Arg Lys Ser Glu Val Val Met Asn Val Leu Asp Val Leu Thr  
180 185 190

Lys Leu Thr Leu Leu Val Leu His Leu Ser Leu Ala Ser Ala Pro Met  
195 200 205

Asp Pro Leu Lys Gly Ile Leu Leu Gly Phe Phe Thr Gly Ile Glu Val  
210 215 220

Val Ile Cys Ala Leu Val Val Val Arg Lys Asp Thr Thr Ser His Thr  
225 230 235 240

Tyr Leu Gln Tyr Ser Gly Val Val Thr Trp Val Ala Met Thr Thr Gln  
 245 250 255  
 Ile Leu Ala Ala Gly Leu Gly Tyr Gly Leu Leu Gly Asp Gly Ile Gly  
 260 265 270  
 Tyr Val Leu Phe Thr Leu Phe Ala Thr Tyr Ser Met Leu Pro Leu Pro  
 275 280 285  
 Leu Thr Trp Ala Ile Leu Ala Gly Leu Gly Thr Ser Leu Leu Gln Val  
 290 295 300  
 Ile Leu Gln Val Val Ile Pro Arg Leu Ala Val Ile Ser Ile Asn Gln  
 305 310 315 320  
 Val Val Ala Gln Ala Val Leu Phe Met Cys Met Asn Thr Ala Gly Ile  
 325 330 335  
 Phe Ile Ser Tyr Leu Ser Asp Arg Ala Gln Arg Gln Ala Phe Leu Glu  
 340 345 350  
 Thr Arg Arg Cys Val Glu Ala Arg Leu Arg Leu Glu Thr Glu Asn Gln  
 355 360 365  
 Arg Gln Glu Arg Leu Val Leu Ser Val Leu Pro Arg Phe Val Val Leu  
 370 375 380  
 Glu Met Ile Asn Asp Met Thr Asn Val Glu Asp Glu His Leu Gln His  
 385 390 395 400  
 Gln Phe His Arg Ile Tyr Ile His Arg Tyr Glu Asn Val Ser Ile Leu  
 405 410 415  
 Phe Ala Asp Val Lys Gly Phe Thr Asn Leu Ser Thr Thr Leu Ser Ala  
 420 425 430  
 Gln Glu Leu Val Arg Met Leu Asn Glu Leu Phe Ala Arg Phe Asp Arg  
 435 440 445  
 Leu Ala His Glu His His Cys Leu Arg Ile Lys Ile Leu Gly Asp Cys  
 450 455 460  
 Tyr Tyr Cys Val Ser Gly Leu Pro Glu Pro Arg Gln Asp His Ala His  
 465 470 475 480  
 Cys Cys Val Glu Met Gly Leu Ser Met Ile Lys Thr Ile Arg Tyr Val  
 485 490 495  
 Arg Ser Arg Thr Lys His Asp Val Asp Met Arg Ile Gly Ile His Ser  
 500 505 510  
 Gly Ser Val Leu Cys Gly Val Leu Gly Leu Arg Lys Trp Gln Phe Asp  
 515 520 525  
 Val Trp Ser Trp Asp Val Asp Ile Ala Asn Lys Leu Glu Ser Gly Gly  
 530 535 540  
 Ile Pro Gly Arg Ile His Ile Ser Lys Ala Thr Leu Asp Cys Leu Asn  
 545 550 555 560

Gly Asp Tyr Asn Val Glu Glu Gly His Gly Lys Glu Arg Asn Glu Phe  
 565 570 575  
 Leu Arg Lys His Asn Ile Glu Thr Tyr Leu Ile Lys Gln Pro Glu Asp  
 580 585 590  
 Ser Leu Leu Ser Leu Pro Glu Asp Ile Val Lys Glu Ser Val Ser Ser  
 595 600 605  
 Ser Asp Arg Arg Asn Ser Gly Ala Thr Phe Thr Glu Gly Ser Trp Ser  
 610 615 620  
 Pro Glu Leu Pro Phe Asp Asn Ile Val Gly Lys Gln Asn Thr Leu Ala  
 625 630 635 640  
 Ala Leu Thr Arg Asn Ser Ile Asn Leu Leu Pro Asn His Leu Ala Gln  
 645 650 655  
 Ala Leu His Val Gln Ser Gly Pro Glu Glu Ile Asn Lys Arg Ile Glu  
 660 665 670  
 His Thr Ile Asp Leu Arg Ser Gly Asp Lys Leu Arg Arg Glu His Ile  
 675 680 685  
 Lys Pro Phe Ser Leu Met Phe Lys Asp Ser Ser Leu Glu His Lys Tyr  
 690 695 700  
 Ser Gln Met Arg Asp Glu Val Phe Lys Ser Asn Leu Val Cys Ala Phe  
 705 710 715 720  
 Ile Val Leu Leu Phe Ile Thr Ala Ile Gln Ser Leu Leu Pro Ser Ser  
 725 730 735  
 Arg Val Met Pro Met Thr Ile Gln Phe Ser Ile Leu Ile Met Leu His  
 740 745 750  
 Ser Ala Leu Val Leu Ile Thr Thr Ala Glu Asp Tyr Lys Cys Leu Pro  
 755 760 765  
 Leu Ile Leu Arg Lys Thr Cys Cys Trp Ile Asn Glu Thr Tyr Leu Ala  
 770 775 780  
 Arg Asn Val Ile Ile Phe Ala Ser Ile Leu Ile Asn Phe Leu Gly Ala  
 785 790 795 800  
 Ile Leu Asn Ile Leu Trp Cys Asp Phe Asp Lys Ser Ile Pro Leu Lys  
 805 810 815  
 Asn Leu Thr Phe Asn Ser Ser Ala Val Phe Thr Asp Ile Cys Ser Tyr  
 820 825 830  
 Pro Glu Tyr Phe Val Phe Thr Gly Val Leu Ala Met Val Thr Cys Ala  
 835 840 845  
 Val Phe Leu Arg Leu Asn Ser Val Leu Lys Leu Ala Val Leu Leu Ile  
 850 855 860  
 Met Ile Ala Ile Tyr Ala Leu Leu Thr Glu Thr Val Tyr Ala Gly Leu  
 865 870 875 880



Phe Leu Arg Tyr Asp Asn Leu Asn His Ser Gly Glu Asp Phe Leu Gly  
 885 890 895  
 Thr Lys Glu Val Ser Leu Leu Leu Met Ala Met Phe Leu Leu Ala Val  
 900 905 910  
 Phe Tyr His Gly Gln Gln Leu Glu Tyr Thr Ala Arg Leu Asp Phe Leu  
 915 920 925  
 Trp Arg Val Gln Ala Lys Glu Glu Ile Asn Glu Met Lys Glu Leu Arg  
 930 935 940  
 Glu His Asn Glu Asn Met Leu Arg Asn Ile Leu Pro Ser His Val Ala  
 945 950 955 960  
 Arg His Phe Leu Glu Lys Asp Arg Asp Asn Glu Glu Leu Tyr Ser Gln  
 965 970 975  
 Ser Tyr Asp Ala Val Gly Val Met Phe Ala Ser Ile Pro Gly Phe Ala  
 980 985 990  
 Asp Phe Tyr Ser Gln Thr Glu Met Asn Asn Gln Gly Val Glu Cys Leu  
 995 1000 1005  
 Arg Leu Leu Asn Glu Ile Ile Ala Asp Phe Asp Glu Leu Leu Gly  
 1010 1015 1020  
 Glu Asp Arg Phe Gln Asp Ile Glu Lys Ile Lys Thr Ile Gly Ser  
 1025 1030 1035  
 Thr Tyr Met Ala Val Ser Gly Leu Ser Pro Glu Lys Gln Gln Cys  
 1040 1045 1050  
 Glu Asp Lys Trp Gly His Leu Cys Ala Leu Ala Asp Phe Ser Leu  
 1055 1060 1065  
 Ala Leu Thr Glu Ser Ile Gln Glu Ile Asn Lys His Ser Phe Asn  
 1070 1075 1080  
 Asn Phe Glu Leu Arg Ile Gly Ile Ser His Gly Ser Val Val Ala  
 1085 1090 1095  
 Gly Val Ile Gly Ala Lys Lys Pro Gln Tyr Asp Ile Trp Gly Lys  
 1100 1105 1110  
 Thr Val Asn Leu Ala Ser Arg Met Asp Ser Thr Gly Val Ser Gly  
 1115 1120 1125  
 Arg Ile Gln Val Pro Glu Glu Thr Tyr Leu Ile Leu Lys Asp Gln  
 1130 1135 1140  
 Gly Phe Ala Phe Asp Tyr Arg Gly Glu Ile Tyr Val Lys Gly Ile  
 1145 1150 1155  
 Ser Glu Gln Glu Gly Lys Ile Lys Thr Tyr Phe Leu Leu Gly Arg  
 1160 1165 1170  
 Val Gln Pro Asn Pro Phe Ile Leu Pro Pro Arg Arg Leu Pro Gly

1175                      1180                      1185

Gln Tyr Ser Leu Ala Ala Val Val Leu Gly Leu Val Gln Ser Leu  
1190                      1195                      1200

Asn Arg Gln Arg Gln Lys Gln Leu Leu Asn Glu Asn Asn Asn Thr  
1205                      1210                      1215

Gly Ile Ile Lys Gly His Tyr Asn Arg Arg Thr Leu Leu Ser Pro  
1220                      1225                      1230

Ser Gly Thr Glu Pro Gly Ala Gln Ala Glu Gly Thr Asp Lys Ser  
1235                      1240                      1245

Asp Leu Pro  
1250

<210> 119  
<211> 143  
<212> PRT  
<213> Homo sapiens

<400> 119

Met Gly Lys Cys Arg Gly Leu Arg Thr Ala Arg Lys Leu Arg Ser His  
1                      5                      10                      15

Arg Arg Asp Gln Lys Trp His Asp Lys Gln Tyr Lys Lys Ala His Leu  
20                      25                      30

Gly Thr Ala Leu Lys Ala Asn Pro Phe Gly Gly Ala Ser His Ala Lys  
35                      40                      45

Gly Ile Val Leu Glu Lys Val Gly Val Glu Ala Lys Gln Pro Asn Ser  
50                      55                      60

Ala Ile Arg Lys Cys Val Arg Val Gln Leu Ile Lys Asn Gly Lys Lys  
65                      70                      75                      80

Ile Thr Ala Phe Val Pro Asn Asp Gly Cys Leu Asn Phe Ile Glu Glu  
85                      90                      95

Asn Asp Glu Val Leu Val Ala Gly Phe Gly Arg Lys Gly His Ala Val  
100                      105                      110

Gly Asp Ile Pro Gly Val Arg Phe Lys Val Val Lys Val Ala Asn Val  
115                      120                      125

Ser Leu Leu Ala Leu Tyr Lys Gly Lys Lys Glu Arg Pro Arg Ser  
130                      135                      140

<210> 120  
<211> 144  
<212> PRT  
<213> Homo sapiens

<400> 120

Met Ala Phe Thr Phe Ala Ala Phe Cys Tyr Met Leu Ala Leu Leu Leu  
1                      5                      10                      15

Thr Ala Ala Leu Ile Phe Phe Ala Ile Trp His Ile Ile Ala Phe Asp  
20                      25                      30

Glu Leu Lys Thr Asp Tyr Lys Asn Pro Ile Asp Gln Cys Asn Thr Leu  
35 40 45

Asn Pro Leu Val Leu Pro Glu Tyr Leu Ile His Ala Phe Phe Cys Val  
50 55 60

Met Phe Leu Cys Ala Ala Glu Trp Leu Thr Leu Gly Leu Asn Met Pro  
65 70 75 80

Leu Leu Ala Tyr His Ile Trp Arg Tyr Met Ser Arg Pro Val Met Ser  
85 90 95

Gly Pro Gly Leu Tyr Asp Pro Thr Thr Ile Met Asn Ala Asp Ile Leu  
100 105 110

Ala Tyr Cys Gln Lys Glu Gly Trp Cys Lys Leu Ala Phe Tyr Leu Leu  
115 120 125

Ala Phe Phe Tyr Tyr Leu Tyr Gly Met Ile Tyr Val Leu Val Ser Ser  
130 135 140

<210> 121  
<211> 1516  
<212> PRT  
<213> Homo sapiens

<400> 121

Met Ala Pro Ala Lys Ala Thr Asn Val Val Arg Leu Leu Leu Gly Ser  
1 5 10 15

Thr Ala Leu Trp Leu Ser Gln Leu Gly Ser Gly Thr Val Ala Ala Ser  
20 25 30

Lys Ser Val Thr Ala His Leu Ala Ala Lys Trp Pro Glu Thr Pro Leu  
35 40 45

Leu Leu Glu Ala Ser Glu Phe Met Ala Glu Glu Ser Asn Glu Lys Phe  
50 55 60

Trp Gln Phe Leu Glu Thr Val Gln Glu Leu Ala Ile Tyr Lys Gln Thr  
65 70 75 80

Glu Ser Asp Tyr Ser Tyr Tyr Asn Leu Ile Leu Lys Lys Ala Gly Gln  
85 90 95

Phe Leu Asp Asn Leu His Ile Asn Leu Leu Lys Phe Ala Phe Ser Ile  
100 105 110

Arg Ala Tyr Ser Pro Ala Ile Gln Met Phe Gln Gln Ile Ala Ala Asp  
115 120 125

Glu Pro Pro Pro Asp Gly Cys Asn Ala Phe Val Val Ile His Lys Lys  
130 135 140

His Thr Cys Lys Ile Asn Glu Ile Lys Lys Leu Leu Lys Lys Ala Ala  
145 150 155 160

Ser Arg Thr Arg Pro Tyr Leu Phe Lys Gly Asp His Lys Phe Pro Thr  
165 170 175

Asn Lys Glu Asn Leu Pro Val Val Ile Leu Tyr Ala Glu Met Gly Thr  
 180 185 190  
 Arg Thr Phe Ser Ala Phe His Lys Val Leu Ser Glu Lys Ala Gln Asn  
 195 200 205  
 Glu Glu Ile Leu Tyr Val Leu Arg His Tyr Ile Gln Lys Pro Ser Ser  
 210 215 220  
 Arg Lys Met Tyr Leu Ser Gly Tyr Gly Val Glu Leu Ala Ile Lys Ser  
 225 230 235 240  
 Thr Glu Tyr Lys Ala Leu Asp Asp Thr Gln Val Lys Thr Val Thr Asn  
 245 250 255  
 Thr Thr Val Glu Asp Glu Thr Glu Thr Asn Glu Val Gln Gly Phe Leu  
 260 265 270  
 Phe Gly Lys Leu Lys Glu Ile Tyr Ser Asp Leu Arg Asp Asn Leu Thr  
 275 280 285  
 Ala Phe His Lys Tyr Leu Ile Glu Ser Asn Lys Gln Met Met Pro Leu  
 290 295 300  
 Lys Val Trp Glu Leu Gln Asp Leu Ser Phe Gln Ala Ala Ser Gln Ile  
 305 310 315 320  
 Met Ser Thr Pro Val Tyr Asp Ala Ile Lys Leu Met Lys Asp Ile Ser  
 325 330 335  
 Gln Asn Phe Pro Ile Lys Ala Arg Ser Leu Thr Arg Ile Ala Val Asn  
 340 345 350  
 Gln His Met Arg Glu Glu Ile Lys Glu Asn Gln Lys Asp Leu Gln Val  
 355 360 365  
 Arg Phe Lys Ile Gln Pro Gly Asp Ala Arg Leu Phe Ile Asn Gly Leu  
 370 375 380  
 Arg Val Asp Met Asp Val Tyr Asp Ala Phe Ser Ile Leu Asp Met Leu  
 385 390 395 400  
 Lys Leu Glu Gly Lys Met Met Asn Gly Leu Arg Asn Leu Gly Ile Asn  
 405 410 415  
 Gly Glu Asp Met Ser Lys Phe Leu Lys Leu Asn Ser His Ile Trp Glu  
 420 425 430  
 Tyr Thr Tyr Val Leu Asp Ile Arg His Ser Ser Ile Met Trp Ile Asn  
 435 440 445  
 Asp Leu Glu Asn Asp Asp Leu Tyr Ile Thr Trp Pro Thr Ser Cys Gln  
 450 455 460  
 Lys Leu Leu Lys Pro Val Phe Pro Gly Ser Val Pro Ser Ile Arg Arg  
 465 470 475 480  
 Asn Phe His Asn Leu Val Leu Phe Ile Asp Pro Ala Gln Glu Tyr Thr

485	490	495
Leu Asp Phe Ile Lys Leu Ala Asp Val Phe Tyr Ser His Glu Val Pro 500 505 510		
Leu Arg Ile Gly Phe Val Phe Ile Leu Asn Thr Asp Asp Glu Val Asp 515 520 525		
Gly Ala Asn Asp Ala Gly Val Ala Leu Trp Arg Ala Phe Asn Tyr Ile 530 535 540		
Ala Glu Glu Phe Asp Ile Ser Glu Ala Phe Ile Ser Ile Val His Met 545 550 555 560		
Tyr Gln Lys Val Lys Lys Asp Gln Asn Ile Leu Thr Val Asp Asn Val 565 570 575		
Lys Ser Val Leu Gln Asn Thr Phe Pro His Ala Asn Ile Trp Asp Ile 580 585 590		
Leu Gly Ile His Ser Lys Tyr Asp Glu Glu Arg Lys Ala Gly Ala Ser 595 600 605		
Phe Tyr Lys Met Thr Gly Leu Gly Pro Leu Pro Gln Ala Leu Tyr Asn 610 615 620		
Gly Glu Pro Phe Lys His Glu Glu Met Asn Ile Lys Glu Leu Lys Met 625 630 635 640		
Ala Val Leu Gln Arg Met Met Asp Ala Ser Val Tyr Leu Gln Arg Glu 645 650 655		
Val Phe Leu Gly Thr Leu Asn Asp Arg Thr Asn Ala Ile Asp Phe Leu 660 665 670		
Met Asp Arg Asn Asn Val Val Pro Arg Ile Asn Thr Leu Ile Leu Arg 675 680 685		
Thr Asn Gln Gln Tyr Leu Asn Leu Ile Ser Thr Ser Val Thr Ala Asp 690 695 700		
Val Glu Asp Phe Ser Thr Phe Phe Phe Leu Asp Ser Gln Asp Lys Ser 705 710 715 720		
Ala Val Ile Ala Lys Asn Met Tyr Tyr Leu Thr Gln Asp Asp Glu Ser 725 730 735		
Ile Ile Ser Ala Val Thr Leu Trp Ile Ile Ala Asp Phe Asp Lys Pro 740 745 750		
Ser Gly Arg Lys Leu Leu Phe Asn Ala Leu Lys His Met Lys Thr Ser 755 760 765		
Val His Ser Arg Leu Gly Ile Ile Tyr Asn Pro Thr Ser Lys Ile Asn 770 775 780		
Glu Glu Asn Thr Ala Ile Ser Arg Gly Ile Leu Ala Ala Phe Leu Thr 785 790 795 800		

Gln Lys Asn Met Phe Leu Arg Ser Phe Leu Gly Gln Leu Ala Lys Glu  
 805 810 815  
 Glu Ile Ala Thr Thr Ile Tyr Ser Gly Asp Lys Ile Lys Thr Phe Leu  
 820 825 830  
 Ile Glu Gly Met Asp Lys Asn Ala Phe Glu Lys Lys Tyr Asn Thr Val  
 835 840 845  
 Gly Val Asn Ile Phe Arg Thr His Gln Leu Phe Cys Gln Asp Val Leu  
 850 855 860  
 Lys Leu Arg Pro Gly Glu Met Gly Ile Val Ser Asn Gly Arg Phe Leu  
 865 870 875 880  
 Gly Pro Leu Asp Glu Asp Phe Tyr Ala Glu Asp Phe Tyr Leu Leu Glu  
 885 890 895  
 Lys Ile Thr Phe Ser Asn Leu Gly Glu Lys Ile Lys Gly Ile Val Glu  
 900 905 910  
 Asn Met Gly Ile Asn Ala Asn Asn Met Ser Asp Phe Ile Met Lys Val  
 915 920 925  
 Asp Ala Leu Met Ser Ser Val Pro Lys Arg Ala Ser Arg Tyr Asp Val  
 930 935 940  
 Thr Phe Leu Arg Glu Asn His Ser Val Ile Lys Thr Asn Pro Gln Glu  
 945 950 955 960  
 Asn Asp Met Phe Phe Asn Val Ile Ala Ile Val Asp Leu Leu Ala Arg  
 965 970 975  
 Glu Ala Gln Lys Met Ala Gln Leu Leu Val Val Leu Gly Lys Ile Ile  
 980 985 990  
 Asn Leu Lys Ile Lys Leu Phe Met Asn Cys Arg Gly Arg Leu Ser Glu  
 995 1000 1005  
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 Phe Leu Asp Ile Pro Glu Ser Pro Leu Leu Ile Leu Asn Met Ile  
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 Thr Pro Glu Gly Trp Leu Val Glu Thr Val His Ser Asn Cys Asp  
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 1070 1075 1080  
 Gly Tyr Glu Leu Glu Tyr Leu Leu Leu Glu Gly Gln Cys Phe Asp  
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 Lys Val Thr Glu Gln Pro Pro Arg Gly Leu Gln Phe Thr Leu Gly  
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Thr Lys Asn Lys Pro Ala Val Val Asp Thr Ile Val Met Ala His  
 1115 1120 1125  
 His Gly Tyr Phe Gln Leu Lys Ala Asn Pro Gly Ala Trp Ile Leu  
 1130 1135 1140  
 Arg Leu His Gln Gly Lys Ser Glu Asp Ile Tyr Gln Ile Val Gly  
 1145 1150 1155  
 His Glu Gly Thr Asp Ser Gln Ala Asp Leu Glu Asp Ile Ile Val  
 1160 1165 1170  
 Val Leu Asn Ser Phe Lys Ser Lys Ile Leu Lys Val Lys Val Lys  
 1175 1180 1185  
 Lys Glu Thr Asp Lys Ile Lys Glu Asp Ile Leu Thr Asp Glu Asp  
 1190 1195 1200  
 Glu Lys Thr Lys Gly Leu Trp Asp Ser Ile Lys Ser Phe Thr Val  
 1205 1210 1215  
 Ser Leu His Lys Glu Asn Lys Lys Glu Lys Asp Val Leu Asn Ile  
 1220 1225 1230  
 Phe Ser Val Ala Ser Gly His Leu Tyr Glu Arg Phe Leu Arg Ile  
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 Met Met Leu Ser Val Leu Arg Asn Thr Lys Thr Pro Val Lys Phe  
 1250 1255 1260  
 Trp Leu Leu Lys Asn Tyr Leu Ser Pro Thr Phe Lys Glu Val Ile  
 1265 1270 1275  
 Pro His Met Ala Lys Glu Tyr Gly Phe Arg Tyr Glu Leu Val Gln  
 1280 1285 1290  
 Tyr Arg Trp Pro Arg Trp Leu Arg Gln Gln Thr Glu Arg Gln Arg  
 1295 1300 1305  
 Ile Ile Trp Gly Tyr Lys Ile Leu Phe Leu Asp Val Leu Phe Pro  
 1310 1315 1320  
 Leu Ala Val Asp Lys Ile Ile Phe Val Asp Ala Asp Gln Ile Val  
 1325 1330 1335  
 Arg His Asp Leu Lys Glu Leu Arg Asp Phe Asp Leu Asp Gly Ala  
 1340 1345 1350  
 Pro Tyr Gly Tyr Thr Pro Phe Cys Asp Ser Arg Arg Glu Met Asp  
 1355 1360 1365  
 Gly Tyr Arg Phe Trp Lys Thr Gly Tyr Trp Ala Ser His Leu Leu  
 1370 1375 1380  
 Arg Arg Lys Tyr His Ile Ser Ala Leu Tyr Val Val Asp Leu Lys  
 1385 1390 1395  
 Lys Phe Arg Arg Ile Gly Ala Gly Asp Arg Leu Arg Ser Gln Tyr  
 1400 1405 1410

Gln Ala Leu Ser Gln Asp Pro Asn Ser Leu Ser Asn Leu Asp Gln  
1415 1420 1425

Asp Leu Pro Asn Asn Met Ile Tyr Gln Val Ala Ile Lys Ser Leu  
1430 1435 1440

Pro Gln Asp Trp Leu Trp Cys Glu Thr Trp Cys Asp Asp Glu Ser  
1445 1450 1455

Lys Gln Arg Ala Lys Thr Ile Asp Leu Cys Asn Asn Pro Lys Thr  
1460 1465 1470

Lys Glu Ser Lys Leu Lys Ala Ala Ala Arg Ile Val Pro Glu Trp  
1475 1480 1485

Val Glu Tyr Asp Ala Glu Ile Arg Gln Leu Leu Asp His Leu Glu  
1490 1495 1500

Asn Lys Lys Gln Asp Thr Ile Leu Thr His Asp Glu Leu  
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<210> 122

<211> 798

<212> PRT

<213> Homo sapiens

<400> 122

Met Asn Leu Gln Pro Ile Phe Trp Ile Gly Leu Ile Ser Ser Val Cys  
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Cys Val Phe Ala Gln Thr Asp Glu Asn Arg Cys Leu Lys Ala Asn Ala  
20 25 30

Lys Ser Cys Gly Glu Cys Ile Gln Ala Gly Pro Asn Cys Gly Trp Cys  
35 40 45

Thr Asn Ser Thr Phe Leu Gln Glu Gly Met Pro Thr Ser Ala Arg Cys  
50 55 60

Asp Asp Leu Glu Ala Leu Lys Lys Lys Gly Cys Pro Pro Asp Asp Ile  
65 70 75 80

Glu Asn Pro Arg Gly Ser Lys Asp Ile Lys Lys Asn Lys Asn Val Thr  
85 90 95

Asn Arg Ser Lys Gly Thr Ala Glu Lys Leu Lys Pro Glu Asp Ile His  
100 105 110

Gln Ile Gln Pro Gln Gln Leu Val Leu Arg Leu Arg Ser Gly Glu Pro  
115 120 125

Gln Thr Phe Thr Leu Lys Phe Lys Arg Ala Glu Asp Tyr Pro Ile Asp  
130 135 140

Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Glu  
145 150 155 160

Asn Val Lys Ser Leu Gly Thr Asp Leu Met Asn Glu Met Arg Arg Ile  
165 170 175



Thr Ser Asp Phe Arg Ile Gly Phe Gly Ser Phe Val Glu Lys Thr Val  
 180 185 190  
 Met Pro Tyr Ile Ser Thr Thr Pro Ala Lys Leu Arg Asn Pro Cys Thr  
 195 200 205  
 Ser Glu Gln Asn Cys Thr Thr Pro Phe Ser Tyr Lys Asn Val Leu Ser  
 210 215 220  
 Leu Thr Asn Lys Gly Glu Val Phe Asn Glu Leu Val Gly Lys Gln Arg  
 225 230 235 240  
 Ile Ser Gly Asn Leu Asp Ser Pro Glu Gly Gly Phe Asp Ala Ile Met  
 245 250 255  
 Gln Val Ala Val Cys Gly Ser Leu Ile Gly Trp Arg Asn Val Thr Arg  
 260 265 270  
 Leu Leu Val Phe Ser Thr Asp Ala Gly Phe His Phe Ala Gly Asp Gly  
 275 280 285  
 Lys Leu Gly Gly Ile Val Leu Pro Asn Asp Gly Gln Cys His Leu Glu  
 290 295 300  
 Asn Asn Met Tyr Thr Met Ser His Tyr Tyr Asp Tyr Pro Ser Ile Ala  
 305 310 315 320  
 His Leu Val Gln Lys Leu Ser Glu Asn Asn Ile Gln Thr Ile Phe Ala  
 325 330 335  
 Val Thr Glu Glu Phe Gln Pro Val Tyr Lys Glu Leu Lys Asn Leu Ile  
 340 345 350  
 Pro Lys Ser Ala Val Gly Thr Leu Ser Ala Asn Ser Ser Asn Val Ile  
 355 360 365  
 Gln Leu Ile Ile Asp Ala Tyr Asn Ser Leu Ser Ser Glu Val Ile Leu  
 370 375 380  
 Glu Asn Gly Lys Leu Ser Glu Gly Val Thr Ile Ser Tyr Lys Ser Tyr  
 385 390 395 400  
 Cys Lys Asn Gly Val Asn Gly Thr Gly Glu Asn Gly Arg Lys Cys Ser  
 405 410 415  
 Asn Ile Ser Ile Gly Asp Glu Val Gln Phe Glu Ile Ser Ile Thr Ser  
 420 425 430  
 Asn Lys Cys Pro Lys Lys Asp Ser Asp Ser Phe Lys Ile Arg Pro Leu  
 435 440 445  
 Gly Phe Thr Glu Glu Val Glu Val Ile Leu Gln Tyr Ile Cys Glu Cys  
 450 455 460  
 Glu Cys Gln Ser Glu Gly Ile Pro Glu Ser Pro Lys Cys His Glu Gly  
 465 470 475 480  
 Asn Gly Thr Phe Glu Cys Gly Ala Cys Arg Cys Asn Glu Gly Arg Val

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<210> 123  
 <211> 317  
 <212> PRT  
 <213> Homo sapiens

<400> 123

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Met Thr Glu Gln Met Thr Leu Arg Gly Thr Leu Lys Gly His Asn Gly
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Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile Leu
20          25          30

Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys Leu Thr Arg Asp
35          40          45

Glu Thr Asn Tyr Gly Ile Pro Gln Arg Ala Leu Arg Gly His Ser His
50          55          60

Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln Phe Ala Leu Ser
65          70          75          80

Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp Leu Thr Thr Gly Thr
85          90          95

Thr Thr Arg Arg Phe Val Gly His Thr Lys Asp Val Leu Ser Val Ala
100         105         110

Phe Ser Ser Asp Asn Arg Gln Ile Val Ser Gly Ser Arg Asp Lys Thr
115         120         125

Ile Lys Leu Trp Asn Thr Leu Gly Val Cys Lys Tyr Thr Val Gln Asp
130         135         140

Glu Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser
145         150         155         160

Ser Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val
165         170         175

Trp Asn Leu Ala Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr
180         185         190

Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala
195         200         205

Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly
210         215         220

Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys
225         230         235         240

Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
245         250         255

Lys Ile Trp Asp Leu Glu Gly Lys Ile Ile Val Asp Glu Leu Lys Gln
260         265         270

Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser
275         280         285

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Leu Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp  
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Asn Leu Val Arg Val Trp Gln Val Thr Ile Gly Thr Arg  
 305 310 315

<210> 124  
 <211> 351  
 <212> PRT  
 <213> Homo sapiens

<400> 124

Met Gln Arg Ala Leu Pro Gly Ala Arg Gln His Leu Gly Ala Ile Leu  
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Ala Ser Ala Ser Val Val Val Lys Ala Leu Cys Ala Ala Val Leu Phe  
 20 25 30

Leu Tyr Leu Leu Ser Phe Ala Val Asp Thr Gly Cys Leu Ala Val Thr  
 35 40 45

Pro Gly Tyr Leu Phe Pro Pro Asn Phe Trp Ile Trp Thr Leu Ala Thr  
 50 55 60

His Gly Leu Met Glu Gln His Val Trp Asp Val Ala Ile Ser Leu Thr  
 65 70 75 80

Thr Val Val Val Ala Gly Arg Leu Leu Glu Pro Leu Trp Gly Ala Leu  
 85 90 95

Glu Leu Leu Ile Phe Phe Ser Val Val Asn Val Ser Val Gly Leu Leu  
 100 105 110

Gly Ala Phe Ala Tyr Leu Leu Thr Tyr Met Ala Ser Phe Asn Leu Val  
 115 120 125

Tyr Leu Phe Thr Val Arg Ile His Gly Ala Leu Gly Phe Leu Gly Gly  
 130 135 140

Val Leu Val Ala Leu Lys Gln Thr Met Gly Asp Cys Val Val Leu Arg  
 145 150 155 160

Val Pro Gln Val Arg Val Ser Val Met Pro Met Leu Leu Leu Ala Leu  
 165 170 175

Leu Leu Leu Leu Arg Leu Ala Thr Leu Leu Gln Ser Pro Ala Leu Ala  
 180 185 190

Ser Tyr Gly Phe Gly Leu Leu Ser Ser Trp Val Tyr Leu Arg Phe Tyr  
 195 200 205

Gln Arg His Ser Arg Gly Arg Gly Asp Met Ala Asp His Phe Ala Phe  
 210 215 220

Ala Thr Phe Phe Pro Glu Ile Leu Gln Pro Val Val Gly Leu Leu Ala  
 225 230 235 240

Asn Leu Val His Ser Leu Leu Val Lys Val Lys Ile Cys Gln Lys Thr  
 245 250 255

Val Lys Arg Tyr Asp Val Gly Ala Pro Ser Ser Ile Thr Ile Ser Leu  
260 265 270

Pro Gly Thr Asp Pro Gln Asp Ala Glu Arg Arg Arg Gln Leu Ala Leu  
275 280 285

Lys Ala Leu Asn Glu Arg Leu Lys Arg Val Glu Asp Gln Ser Ile Trp  
290 295 300

Pro Ser Met Asp Asp Asp Glu Glu Glu Ser Gly Ala Lys Val Asp Ser  
305 310 315 320

Pro Leu Pro Ser Asp Lys Ala Pro Thr Pro Pro Gly Lys Gly Ala Ala  
325 330 335

Pro Glu Ser Ser Leu Ile Thr Phe Glu Ala Ala Pro Pro Thr Leu  
340 345 350

<210> 125

<211> 310

<212> PRT

<213> Homo sapiens

<400> 125

Met Arg Arg Ala Ala Leu Trp Leu Trp Leu Cys Ala Leu Ala Leu Ser  
1 5 10 15

Leu Gln Leu Ala Leu Pro Gln Ile Val Ala Thr Asn Leu Pro Pro Glu  
20 25 30

Asp Gln Asp Gly Ser Gly Asp Asp Ser Asp Asn Phe Ser Gly Ser Gly  
35 40 45

Ala Gly Ala Leu Gln Asp Ile Thr Leu Ser Gln Gln Thr Pro Ser Thr  
50 55 60

Trp Lys Asp Thr Gln Leu Leu Thr Ala Ile Pro Thr Ser Pro Glu Pro  
65 70 75 80

Thr Gly Leu Glu Ala Thr Ala Ala Ser Thr Ser Thr Leu Pro Ala Gly  
85 90 95

Glu Gly Pro Lys Glu Gly Glu Ala Val Val Leu Pro Glu Val Glu Pro  
100 105 110

Gly Leu Thr Ala Arg Glu Gln Glu Ala Thr Pro Arg Pro Arg Glu Thr  
115 120 125

Thr Gln Leu Pro Thr Thr His Gln Ala Ser Thr Thr Thr Ala Thr Thr  
130 135 140

Ala Gln Glu Pro Ala Thr Ser His Pro His Arg Asp Met Gln Pro Gly  
145 150 155 160

His His Glu Thr Ser Thr Pro Ala Gly Pro Ser Gln Ala Asp Leu His  
165 170 175

Thr Pro His Thr Glu Asp Gly Gly Pro Ser Ala Thr Glu Arg Ala Ala  
180 185 190

Glu Asp Gly Ala Ser Ser Gln Leu Pro Ala Ala Glu Gly Ser Gly Glu  
195 200 205

Gln Asp Phe Thr Phe Glu Thr Ser Gly Glu Asn Thr Ala Val Val Ala  
210 215 220

Val Glu Pro Asp Arg Arg Asn Gln Ser Pro Val Asp Gln Gly Ala Thr  
225 230 235 240

Gly Ala Ser Gln Gly Leu Leu Asp Arg Lys Glu Val Leu Gly Gly Val  
245 250 255

Ile Ala Gly Gly Leu Val Gly Leu Ile Phe Ala Val Cys Leu Val Gly  
260 265 270

Phe Met Leu Tyr Arg Met Lys Lys Lys Asp Glu Gly Ser Tyr Ser Leu  
275 280 285

Glu Glu Pro Lys Gln Ala Asn Gly Gly Ala Tyr Gln Lys Pro Thr Lys  
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Gln Glu Glu Phe Tyr Ala  
305 310

<210> 126  
<211> 2174  
<212> PRT  
<213> Homo sapiens

<400> 126

Met Ser Ala Ser Phe Val Pro Asn Gly Ala Ser Leu Glu Asp Cys His  
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Cys Asn Leu Phe Cys Leu Ala Asp Leu Thr Gly Ile Lys Trp Lys Lys  
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Tyr Val Trp Gln Gly Pro Thr Ser Ala Pro Ile Leu Phe Pro Val Thr  
35 40 45

Glu Glu Asp Pro Ile Leu Ser Ser Phe Ser Arg Cys Leu Lys Ala Asp  
50 55 60

Val Leu Gly Val Trp Arg Arg Asp Gln Arg Pro Gly Arg Arg Glu Leu  
65 70 75 80

Trp Ile Phe Trp Trp Gly Glu Asp Pro Val Leu Leu Thr Leu Phe Thr  
85 90 95

Met Thr Tyr Gln Lys Lys Lys Met Glu Cys Gly Arg Met Asp Phe Pro  
100 105 110

Met Asn Ala Val Leu Cys Phe Ser Lys Ala Val His Asn Leu Leu Glu  
115 120 125

Arg Cys Leu Met Asn Arg Asn Phe Val Arg Ile Gly Lys Trp Phe Val  
130 135 140

Lys Pro Tyr Glu Lys Asp Glu Lys Pro Ile Asn Lys Ser Glu His Leu  
145 150 155 160

Ser Cys Ser Phe Thr Phe Phe Leu His Gly Asp Ser Asn Val Cys Thr  
 165 170 175  
 Ser Val Glu Ile Asn Gln His Gln Pro Val Tyr Leu Leu Ser Glu Glu  
 180 185 190  
 His Ile Thr Leu Ala Gln Gln Ser Asn Ser Pro Phe Gln Val Ile Leu  
 195 200 205  
 Cys Pro Phe Gly Leu Asn Gly Thr Leu Thr Gly Gln Ala Phe Lys Met  
 210 215 220  
 Ser Asp Ser Ala Thr Lys Lys Leu Ile Gly Glu Trp Lys Gln Phe Tyr  
 225 230 235 240  
 Pro Ile Ser Cys Cys Leu Lys Glu Met Ser Glu Glu Lys Gln Glu Asp  
 245 250 255  
 Met Asp Trp Glu Asp Asp Ser Leu Ala Ala Val Glu Val Leu Val Ala  
 260 265 270  
 Gly Val Arg Met Ile Tyr Pro Ala Cys Phe Val Leu Val Pro Gln Ser  
 275 280 285  
 Asp Ile Pro Thr Pro Ser Pro Val Gly Ser Thr His Cys Ser Ser Ser  
 290 295 300  
 Cys Leu Gly Val His Gln Val Pro Ala Ser Thr Arg Asp Pro Ala Met  
 305 310 315 320  
 Ser Ser Val Thr Leu Thr Pro Pro Thr Ser Pro Glu Glu Val Gln Thr  
 325 330 335  
 Val Asp Pro Gln Ser Val Gln Lys Trp Val Lys Phe Ser Ser Val Ser  
 340 345 350  
 Asp Gly Phe Asn Ser Asp Ser Thr Ser His His Gly Gly Lys Ile Pro  
 355 360 365  
 Arg Lys Leu Ala Asn His Val Val Asp Arg Val Trp Gln Glu Cys Asn  
 370 375 380  
 Met Asn Arg Ala Gln Asn Lys Lys Lys Tyr Ser Ala Ser Ser Gly Gly  
 385 390 395 400  
 Leu Cys Glu Glu Ala Thr Ala Ala Lys Val Ala Ser Trp Asp Phe Val  
 405 410 415  
 Glu Ala Thr Gln Arg Thr Asn Cys Ser Cys Leu Arg His Lys Asn Leu  
 420 425 430  
 Lys Ser Arg Asn Ala Gly Gln Gln Gly Gln Ala Pro Ser Leu Gly Gln  
 435 440 445  
 Gln Gln Gln Ile Leu Pro Lys His Lys Thr Asn Glu Lys Gln Glu Lys  
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 Ser Glu Glu Pro Gln Lys Arg Pro Leu Thr Pro Phe His His Arg Val  
 465 470 475 480

Ser Val Ser Asp Asp Val Gly Met Asp Ala Asp Ser Ala Ser Gln Arg  
 485 490 495  
 Leu Val Ile Ser Ala Pro Asp Ser Gln Val Arg Phe Ser Asn Ile Arg  
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 Thr Asn Asp Val Ala Lys Thr Pro Gln Met His Gly Thr Glu Met Ala  
 515 520 525  
 Asn Ser Pro Gln Pro Pro Pro Leu Ser Pro His Pro Cys Asp Val Val  
 530 535 540  
 Asp Glu Gly Val Thr Lys Thr Pro Ser Thr Pro Gln Ser Gln His Phe  
 545 550 555 560  
 Tyr Gln Met Pro Thr Pro Asp Pro Leu Val Pro Ser Lys Pro Met Glu  
 565 570 575  
 Asp Arg Ile Asp Ser Leu Ser Gln Ser Phe Pro Pro Gln Tyr Gln Glu  
 580 585 590  
 Ala Val Glu Pro Thr Val Tyr Val Gly Thr Ala Val Asn Leu Glu Glu  
 595 600 605  
 Asp Glu Ala Asn Ile Ala Trp Lys Tyr Tyr Lys Phe Pro Lys Lys Lys  
 610 615 620  
 Asp Val Glu Phe Leu Pro Pro Gln Leu Pro Ser Asp Lys Phe Lys Asp  
 625 630 635 640  
 Asp Pro Val Gly Pro Phe Gly Gln Glu Ser Val Thr Ser Val Thr Glu  
 645 650 655  
 Leu Met Val Gln Cys Lys Lys Pro Leu Lys Val Ser Asp Glu Leu Val  
 660 665 670  
 Gln Gln Tyr Gln Ile Lys Asn Gln Cys Leu Ser Ala Ile Ala Ser Asp  
 675 680 685  
 Ala Glu Gln Glu Pro Lys Ile Asp Pro Tyr Ala Phe Val Glu Gly Asp  
 690 695 700  
 Glu Glu Phe Leu Phe Pro Asp Lys Lys Asp Arg Gln Asn Ser Glu Arg  
 705 710 715 720  
 Glu Ala Gly Lys Lys His Lys Val Glu Asp Gly Thr Ser Ser Val Thr  
 725 730 735  
 Val Leu Ser His Glu Glu Asp Ala Met Ser Leu Phe Ser Pro Ser Ile  
 740 745 750  
 Lys Gln Asp Ala Pro Arg Pro Thr Ser His Ala Arg Pro Pro Ser Thr  
 755 760 765  
 Ser Leu Ile Tyr Asp Ser Asp Leu Ala Val Ser Tyr Thr Asp Leu Asp  
 770 775 780  
 Asn Leu Phe Asn Ser Asp Glu Asp Glu Leu Thr Pro Gly Ser Lys Arg  
 785 790 795 800



Ser Ala Asn Gly Ser Asp Asp Lys Ala Ser Cys Lys Glu Ser Lys Thr  
 805 810 815  
 Gly Asn Leu Asp Pro Leu Ser Cys Ile Ser Thr Ala Asp Leu His Lys  
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 Met Tyr Pro Thr Pro Pro Ser Leu Glu Gln His Ile Met Gly Phe Ser  
 835 840 845  
 Pro Met Asn Met Asn Asn Lys Glu Tyr Gly Ser Met Asp Thr Thr Pro  
 850 855 860  
 Gly Gly Thr Val Leu Glu Gly Asn Ser Ser Ser Ile Gly Ala Gln Phe  
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 Lys Ile Glu Val Asp Glu Gly Phe Cys Ser Pro Lys Pro Ser Glu Ile  
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 Lys Asp Phe Ser Tyr Val Tyr Lys Pro Glu Asn Cys Gln Ile Leu Val  
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 Gly Cys Ser Met Phe Ala Pro Leu Lys Thr Leu Pro Ser Gln Tyr Leu  
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 Pro Leu Ile Lys Leu Pro Glu Glu Cys Ile Tyr Arg Gln Ser Trp Thr  
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 Val Gly Lys Leu Glu Leu Leu Ser Ser Gly Pro Ser Met Pro Phe Ile  
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 Lys Glu Gly Asp Gly Ser Asn Met Asp Gln Glu Tyr Gly Thr Ala Tyr  
 965 970 975  
 Thr Pro Gln Thr His Thr Ser Cys Gly Met Pro Pro Ser Ser Ala Pro  
 980 985 990  
 Pro Ser Asn Ser Gly Ala Gly Ile Leu Pro Ser Pro Ser Thr Pro Arg  
 995 1000 1005  
 Phe Pro Thr Pro Arg Thr Pro Arg Thr Pro Arg Thr Pro Arg Gly  
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 Ala Gly Gly Pro Ala Ser Ala Gln Gly Ser Val Lys Tyr Glu Asn  
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 Ser Asp Leu Tyr Ser Pro Ala Ser Thr Pro Ser Thr Cys Arg Pro  
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 Leu Asn Ser Val Glu Pro Ala Thr Val Pro Ser Ile Pro Glu Ala  
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 His Ser Leu Tyr Val Asn Leu Ile Leu Ser Glu Ser Val Met Asn  
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 Leu Phe Lys Asp Cys Asn Ser Asp Ser Cys Cys Ile Cys Val Cys  
 1085 1090 1095  
 Asn Met Asn Ile Lys Gly Ala Asp Val Gly Val Tyr Ile Pro Asp

1100	1105	1110
Pro Thr Gln Glu Ala Gln Tyr 1115	Arg Cys Thr Cys Gly 1120	Phe Ser Ala 1125
Val Met Asn Arg Lys Phe Gly 1130	Asn Asn Ser Gly Leu 1135	Phe Leu Glu 1140
Asp Glu Leu Asp Ile Ile Gly 1145	Arg Asn Thr Asp Cys 1150	Gly Lys Glu 1155
Ala Glu Lys Arg Phe Glu Ala 1160	Leu Arg Ala Thr Ser 1165	Ala Glu His 1170
Val Asn Gly Gly Leu Lys Glu 1175	Ser Glu Lys Leu Ser 1180	Asp Asp Leu 1185
Ile Leu Leu Leu Gln Asp Gln 1190	Cys Thr Asn Leu Phe 1195	Ser Pro Phe 1200
Gly Ala Ala Asp Gln Asp Pro 1205	Phe Pro Lys Ser Gly 1210	Val Ile Ser 1215
Asn Trp Val Arg Val Glu Glu 1220	Arg Asp Cys Cys Asn 1225	Asp Cys Tyr 1230
Leu Ala Leu Glu His Gly Arg 1235	Gln Phe Met Asp Asn 1240	Met Ser Gly 1245
Gly Lys Val Asp Glu Ala Leu 1250	Val Lys Ser Ser Cys 1255	Leu His Pro 1260
Trp Ser Lys Arg Asn Asp Val 1265	Ser Met Gln Cys Ser 1270	Gln Asp Ile 1275
Leu Arg Met Leu Leu Ser Leu 1280	Gln Pro Val Leu Gln 1285	Asp Ala Ile 1290
Gln Lys Lys Arg Thr Val Arg 1295	Pro Trp Gly Val Gln 1300	Gly Pro Leu 1305
Thr Trp Gln Gln Phe His Lys 1310	Met Ala Gly Arg Gly 1315	Ser Tyr Gly 1320
Thr Asp Glu Ser Pro Glu Pro 1325	Leu Pro Ile Pro Thr 1330	Phe Leu Leu 1335
Gly Tyr Asp Tyr Asp Tyr Leu 1340	Val Leu Ser Pro Phe 1345	Ala Leu Pro 1350
Tyr Trp Glu Arg Leu Met Leu 1355	Glu Pro Tyr Gly Ser 1360	Gln Arg Asp 1365
Ile Ala Tyr Val Val Leu Cys 1370	Pro Glu Asn Glu Ala 1375	Leu Leu Asn 1380
Gly Ala Lys Ser Phe Phe Arg 1385	Asp Leu Thr Ala Ile 1390	Tyr Glu Ser 1395

Cys Arg Leu Gly Gln His Arg Pro Val Ser Arg Leu Leu Thr Asp  
 1400 1405 1410  
 Gly Ile Met Arg Val Gly Ser Thr Ala Ser Lys Lys Leu Ser Glu  
 1415 1420 1425  
 Lys Leu Val Ala Glu Trp Phe Ser Gln Ala Ala Asp Gly Asn Asn  
 1430 1435 1440  
 Glu Ala Phe Ser Lys Leu Lys Leu Tyr Ala Gln Val Cys Arg Tyr  
 1445 1450 1455  
 Asp Leu Gly Pro Tyr Leu Ala Ser Leu Pro Leu Asp Ser Ser Leu  
 1460 1465 1470  
 Leu Ser Gln Pro Asn Leu Val Ala Pro Thr Ser Gln Ser Leu Ile  
 1475 1480 1485  
 Thr Pro Pro Gln Met Thr Asn Thr Gly Asn Ala Asn Thr Pro Ser  
 1490 1495 1500  
 Ala Thr Leu Ala Ser Ala Ala Ser Ser Thr Met Thr Val Thr Ser  
 1505 1510 1515  
 Gly Val Ala Ile Ser Thr Ser Val Ala Thr Ala Asn Ser Thr Leu  
 1520 1525 1530  
 Thr Thr Ala Ser Thr Ser Ser Ser Ser Ser Asn Leu Asn Ser  
 1535 1540 1545  
 Gly Val Ser Ser Asn Lys Leu Pro Ser Phe Pro Pro Phe Gly Ser  
 1550 1555 1560  
 Met Asn Ser Asn Ala Ala Gly Ser Met Ser Thr Gln Ala Asn Thr  
 1565 1570 1575  
 Val Gln Ser Gly Gln Leu Gly Gly Gln Gln Thr Ser Ala Leu Gln  
 1580 1585 1590  
 Thr Ala Gly Ile Ser Gly Glu Ser Ser Ser Leu Pro Thr Gln Pro  
 1595 1600 1605  
 His Pro Asp Val Ser Glu Ser Thr Met Asp Arg Asp Lys Val Gly  
 1610 1615 1620  
 Ile Pro Thr Asp Gly Asp Ser His Ala Val Thr Tyr Pro Pro Ala  
 1625 1630 1635  
 Ile Val Val Tyr Ile Ile Asp Pro Phe Thr Tyr Glu Asn Thr Asp  
 1640 1645 1650  
 Glu Ser Thr Asn Ser Ser Ser Val Trp Thr Leu Gly Leu Leu Arg  
 1655 1660 1665  
 Cys Phe Leu Glu Met Val Gln Thr Leu Pro Pro His Ile Lys Ser  
 1670 1675 1680  
 Thr Val Ser Val Gln Ile Ile Pro Cys Gln Tyr Leu Leu Gln Pro  
 1685 1690 1695

Val Lys His Glu Asp Arg Glu Ile Tyr Pro Gln His Leu Lys Ser  
 1700 1705 1710  
 Leu Ala Phe Ser Ala Phe Thr Gln Cys Arg Arg Pro Leu Pro Thr  
 1715 1720 1725  
 Ser Thr Asn Val Lys Thr Leu Thr Gly Phe Gly Pro Gly Leu Ala  
 1730 1735 1740  
 Met Glu Thr Ala Leu Arg Ser Pro Asp Arg Pro Glu Cys Ile Arg  
 1745 1750 1755  
 Leu Tyr Ala Pro Pro Phe Ile Leu Ala Pro Val Lys Asp Lys Gln  
 1760 1765 1770  
 Thr Glu Leu Gly Glu Thr Phe Gly Glu Ala Gly Gln Lys Tyr Asn  
 1775 1780 1785  
 Val Leu Phe Val Gly Tyr Cys Leu Ser His Asp Gln Arg Trp Ile  
 1790 1795 1800  
 Leu Ala Ser Cys Thr Asp Leu Tyr Gly Glu Leu Leu Glu Thr Cys  
 1805 1810 1815  
 Ile Ile Asn Ile Asp Val Pro Asn Arg Ala Arg Arg Lys Lys Ser  
 1820 1825 1830  
 Ser Ala Arg Lys Phe Gly Leu Gln Lys Leu Trp Glu Trp Cys Leu  
 1835 1840 1845  
 Gly Leu Val Gln Met Ser Ser Leu Pro Trp Arg Val Val Ile Gly  
 1850 1855 1860  
 Arg Leu Gly Arg Ile Gly His Gly Glu Leu Lys Asp Trp Ser Cys  
 1865 1870 1875  
 Leu Leu Ser Arg Arg Asn Leu Gln Ser Leu Ser Lys Arg Leu Lys  
 1880 1885 1890  
 Asp Met Cys Arg Met Cys Gly Ile Ser Ala Ala Asp Ser Pro Ser  
 1895 1900 1905  
 Ile Leu Ser Ala Cys Leu Val Ala Met Glu Pro Gln Gly Ser Phe  
 1910 1915 1920  
 Val Ile Met Pro Asp Ser Val Ser Thr Gly Ser Val Phe Gly Arg  
 1925 1930 1935  
 Ser Thr Thr Leu Asn Met Gln Thr Ser Gln Leu Asn Thr Pro Gln  
 1940 1945 1950  
 Asp Thr Ser Cys Thr His Ile Leu Val Phe Pro Thr Ser Ala Ser  
 1955 1960 1965  
 Val Gln Val Ala Ser Ala Thr Tyr Thr Thr Glu Asn Leu Asp Leu  
 1970 1975 1980  
 Ala Phe Asn Pro Asn Asn Asp Gly Ala Asp Gly Met Gly Ile Phe  
 1985 1990 1995

Asp Leu Leu Asp Thr Gly Asp Asp Leu Asp Pro Asp Ile Ile Asn  
 2000 2005 2010  
 Ile Leu Pro Ala Ser Pro Thr Gly Ser Pro Val His Ser Pro Gly  
 2015 2020 2025  
 Ser His Tyr Pro His Gly Gly Asp Ala Gly Lys Gly Gln Ser Thr  
 2030 2035 2040  
 Asp Arg Leu Leu Ser Thr Glu Pro His Glu Glu Val Pro Asn Ile  
 2045 2050 2055  
 Leu Gln Gln Pro Leu Ala Leu Gly Tyr Phe Val Ser Thr Ala Lys  
 2060 2065 2070  
 Ala Gly Pro Leu Pro Asp Trp Phe Trp Ser Ala Cys Pro Gln Ala  
 2075 2080 2085  
 Gln Tyr Gln Cys Pro Leu Phe Leu Lys Ala Ser Leu His Leu His  
 2090 2095 2100  
 Val Pro Ser Val Gln Ser Asp Glu Leu Leu His Ser Lys His Ser  
 2105 2110 2115  
 His Pro Leu Asp Ser Asn Gln Thr Ser Asp Val Leu Arg Phe Val  
 2120 2125 2130  
 Leu Glu Gln Tyr Asn Ala Leu Ser Trp Leu Thr Cys Asp Pro Ala  
 2135 2140 2145  
 Thr Gln Asp Arg Arg Ser Cys Leu Pro Ile His Phe Val Val Leu  
 2150 2155 2160  
 Asn Gln Leu Tyr Asn Phe Ile Met Asn Met Leu  
 2165 2170  
 <210> 127  
 <211> 415  
 <212> PRT  
 <213> Homo sapiens  
 <400> 127  
 Met Glu Leu Arg Val Gly Asn Arg Tyr Arg Leu Gly Arg Lys Ile Gly  
 1 5 10 15  
 Ser Gly Ser Phe Gly Asp Ile Tyr Leu Gly Thr Asp Ile Ala Ala Gly  
 20 25 30  
 Glu Glu Val Ala Ile Lys Leu Glu Cys Val Lys Thr Lys His Pro Gln  
 35 40 45  
 Leu His Ile Glu Ser Lys Ile Tyr Lys Met Met Gln Gly Gly Val Gly  
 50 55 60  
 Ile Pro Thr Ile Arg Trp Cys Gly Ala Glu Gly Asp Tyr Asn Val Met  
 65 70 75 80  
 Val Met Glu Leu Leu Gly Pro Ser Leu Glu Asp Leu Phe Asn Phe Cys  
 85 90 95

Ser Arg Lys Phe Ser Leu Lys Thr Val Leu Leu Leu Ala Asp Gln Met  
 100 105 110  
 Ile Ser Arg Ile Glu Tyr Ile His Ser Lys Asn Phe Ile His Arg Asp  
 115 120 125  
 Val Lys Pro Asp Asn Phe Leu Met Gly Leu Gly Lys Lys Gly Asn Leu  
 130 135 140  
 Val Tyr Ile Ile Asp Phe Gly Leu Ala Lys Lys Tyr Arg Asp Ala Arg  
 145 150 155 160  
 Thr His Gln His Ile Pro Tyr Arg Glu Asn Lys Asn Leu Thr Gly Thr  
 165 170 175  
 Ala Arg Tyr Ala Ser Ile Asn Thr His Leu Gly Ile Glu Gln Ser Arg  
 180 185 190  
 Arg Asp Asp Leu Glu Ser Leu Gly Tyr Val Leu Met Tyr Phe Asn Leu  
 195 200 205  
 Gly Ser Leu Pro Trp Gln Gly Leu Lys Ala Ala Thr Lys Arg Gln Lys  
 210 215 220  
 Tyr Glu Arg Ile Ser Glu Lys Lys Met Ser Thr Pro Ile Glu Val Leu  
 225 230 235 240  
 Cys Lys Gly Tyr Pro Ser Glu Phe Ala Thr Tyr Leu Asn Phe Cys Arg  
 245 250 255  
 Ser Leu Arg Phe Asp Asp Lys Pro Asp Tyr Ser Tyr Leu Arg Gln Leu  
 260 265 270  
 Phe Arg Asn Leu Phe His Arg Gln Gly Phe Ser Tyr Asp Tyr Val Phe  
 275 280 285  
 Asp Trp Asn Met Leu Lys Phe Gly Ala Ser Arg Ala Ala Asp Asp Ala  
 290 295 300  
 Glu Arg Glu Arg Arg Asp Arg Glu Glu Arg Leu Arg His Ser Arg Asn  
 305 310 315 320  
 Pro Ala Thr Arg Gly Leu Pro Ser Thr Asp Ser Gly Arg Leu Arg Gly  
 325 330 335  
 Thr Gln Glu Val Ala Pro Pro Thr Pro Leu Thr Pro Thr Ser His Thr  
 340 345 350  
 Ala Asn Thr Ser Pro Arg Pro Val Ser Gly Met Glu Arg Glu Arg Lys  
 355 360 365  
 Val Ser Met Arg Leu His Arg Gly Ala Pro Val Asn Ile Ser Ser Ser  
 370 375 380  
 Asp Leu Thr Gly Arg Gln Asp Thr Ser Arg Met Ser Thr Ser Gln Ile  
 385 390 395 400  
 Pro Gly Arg Val Ala Ser Ser Gly Leu Gln Ser Val Val His Arg

405 410 415

<210> 128  
 <211> 204  
 <212> PRT  
 <213> Homo sapiens

<400> 128

Met Thr Glu Trp Glu Thr Ala Ala Pro Ala Val Ala Glu Thr Pro Asp  
 1 5 10 15

Ile Lys Leu Phe Gly Lys Trp Ser Thr Asp Asp Val Gln Ile Asn Asp  
 20 25 30

Ile Ser Leu Gln Asp Tyr Ile Ala Val Lys Glu Lys Tyr Ala Lys Tyr  
 35 40 45

Leu Pro His Ser Ala Gly Arg Tyr Ala Ala Asn Ala Phe Arg Lys Ala  
 50 55 60

Gln Cys Pro Ile Val Glu Arg Leu Thr Asn Ser Met Met Met His Gly  
 65 70 75 80

Arg Asn Asn Gly Lys Lys Leu Met Thr Val Arg Ile Val Lys His Ala  
 85 90 95

Phe Glu Ile Ile His Leu Leu Thr Gly Glu Asn Pro Leu Gln Val Leu  
 100 105 110

Val Asn Ala Ile Ile Asn Ser Gly Pro Arg Glu Asp Ser Thr Arg Ile  
 115 120 125

Gly Arg Ala Gly Thr Val Arg Arg Gln Ala Val Asp Val Ser Pro Leu  
 130 135 140

Arg Arg Val Asn Gln Ala Ile Trp Leu Leu Cys Thr Gly Ala Arg Glu  
 145 150 155 160

Ala Ala Phe Arg Asn Ile Lys Thr Ile Ala Glu Cys Leu Ala Asp Glu  
 165 170 175

Leu Ile Asn Ala Ala Lys Gly Ser Ser Asn Ser Tyr Ala Ile Lys Lys  
 180 185 190

Lys Asp Glu Leu Glu Arg Val Ala Lys Ser Asn Arg  
 195 200

<210> 129  
 <211> 694  
 <212> PRT  
 <213> Homo sapiens

<400> 129

Met Glu Asn Lys Ser Leu Glu Ser Ser Gln Thr Asp Leu Lys Leu Val  
 1 5 10 15

Ala His Pro Arg Ala Lys Ser Lys Val Trp Lys Tyr Phe Gly Phe Asp  
 20 25 30

Thr Asn Ala Glu Gly Cys Ile Leu Gln Trp Lys Lys Ile Tyr Cys Arg  
 35 40 45

Ile Cys Met Ala Gln Ile Ala Tyr Ser Gly Asn Thr Ser Asn Leu Ser  
 50 55 60  
 Tyr His Leu Glu Lys Asn His Pro Glu Glu Phe Cys Glu Phe Val Lys  
 65 70 75 80  
 Ser Asn Thr Glu Gln Met Arg Glu Ala Phe Ala Thr Ala Phe Ser Lys  
 85 90 95  
 Leu Lys Pro Glu Ser Ser Gln Gln Pro Gly Gln Asp Ala Leu Ala Val  
 100 105 110  
 Lys Ala Gly His Gly Tyr Asp Ser Lys Lys Gln Gln Glu Leu Thr Ala  
 115 120 125  
 Ala Val Leu Gly Leu Ile Cys Glu Gly Leu Tyr Pro Ala Ser Ile Val  
 130 135 140  
 Asp Glu Pro Thr Phe Lys Val Leu Leu Lys Thr Ala Asp Pro Arg Tyr  
 145 150 155 160  
 Glu Leu Pro Ser Arg Lys Tyr Ile Ser Thr Lys Ala Ile Pro Glu Lys  
 165 170 175  
 Tyr Gly Ala Val Arg Glu Val Ile Leu Lys Glu Leu Ala Glu Ala Thr  
 180 185 190  
 Trp Cys Gly Ile Ser Thr Asp Met Trp Arg Ser Glu Asn Gln Asn Arg  
 195 200 205  
 Ala Tyr Val Thr Leu Ala Ala His Phe Leu Gly Leu Gly Ala Pro Asn  
 210 215 220  
 Cys Leu Ser Met Gly Ser Arg Cys Leu Lys Thr Phe Glu Val Pro Glu  
 225 230 235 240  
 Glu Asn Thr Ala Glu Thr Ile Thr Arg Val Leu Tyr Glu Val Phe Ile  
 245 250 255  
 Glu Trp Gly Ile Ser Ala Lys Val Phe Gly Ala Thr Thr Asn Tyr Gly  
 260 265 270  
 Lys Asp Ile Val Lys Ala Cys Ser Leu Leu Asp Val Ala Val His Met  
 275 280 285  
 Pro Cys Leu Gly His Thr Phe Asn Ala Gly Ile Gln Gln Ala Phe Gln  
 290 295 300  
 Leu Pro Lys Leu Gly Ala Leu Leu Ser Arg Cys Arg Lys Leu Val Glu  
 305 310 315 320  
 Tyr Phe Gln Gln Ser Ala Val Ala Met Tyr Met Leu Tyr Glu Lys Gln  
 325 330 335  
 Lys Gln Gln Asn Val Ala His Cys Met Leu Val Ser Asn Arg Val Ser  
 340 345 350  
 Trp Trp Gly Ser Thr Leu Ala Met Leu Gln Arg Leu Lys Glu Gln Gln



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355          360          365
Phe Val Ile Ala Gly Val Leu Val Glu Asp Ser Asn Asn His His Leu
370          375          380
Met Leu Glu Ala Ser Glu Trp Ala Thr Ile Glu Gly Leu Val Glu Leu
385          390          395          400
Leu Gln Pro Phe Lys Gln Val Ala Glu Met Leu Ser Ala Ser Arg Tyr
405          410          415
Pro Thr Ile Ser Met Val Lys Pro Leu Leu His Met Leu Leu Asn Thr
420          425          430
Thr Leu Asn Ile Lys Glu Thr Asp Ser Lys Glu Leu Ser Met Ala Lys
435          440          445
Glu Val Ile Ala Lys Glu Leu Ser Lys Thr Tyr Gln Glu Thr Pro Glu
450          455          460
Ile Asp Met Phe Leu Asn Val Ala Thr Phe Leu Asp Pro Arg Tyr Lys
465          470          475          480
Arg Leu Pro Phe Leu Ser Ala Phe Glu Arg Gln Gln Val Glu Asn Arg
485          490          495
Val Val Glu Glu Ala Lys Gly Leu Leu Asp Lys Val Lys Asp Gly Gly
500          505          510
Tyr Arg Pro Ala Glu Asp Lys Ile Phe Pro Val Pro Glu Glu Pro Pro
515          520          525
Val Lys Lys Leu Met Arg Thr Ser Thr Pro Pro Pro Ala Ser Val Ile
530          535          540
Asn Asn Met Leu Ala Glu Ile Phe Cys Gln Thr Gly Gly Val Glu Asp
545          550          555          560
Gln Glu Glu Trp His Ala Gln Val Val Glu Glu Leu Ser Asn Phe Lys
565          570          575
Ser Gln Lys Val Leu Gly Leu Asn Glu Asp Pro Leu Lys Trp Trp Ser
580          585          590
Asp Arg Leu Ala Leu Phe Pro Leu Leu Pro Lys Val Leu Gln Lys Tyr
595          600          605
Trp Cys Val Thr Ala Thr Arg Val Ala Pro Glu Arg Leu Phe Gly Ser
610          615          620
Ala Ala Asn Val Val Ser Ala Lys Arg Asn Arg Leu Ala Pro Ala His
625          630          635          640
Val Asp Glu Gln Val Phe Leu Tyr Glu Asn Ala Arg Ser Gly Ala Glu
645          650          655
Ala Glu Pro Glu Asp Gln Asp Glu Gly Glu Trp Gly Leu Asp Gln Glu
660          665          670

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Gln Val Phe Ser Leu Gly Asp Gly Val Ser Gly Gly Phe Phe Gly Ile  
 675 680 685

Arg Asp Ser Ser Phe Leu  
 690

<210> 130  
 <211> 729  
 <212> PRT  
 <213> Homo sapiens

<400> 130

Met Gly Lys Lys Tyr Lys Asn Ile Val Leu Leu Lys Gly Leu Glu Val  
 1 5 10 15

Ile Asn Asp Tyr His Phe Arg Met Val Lys Ser Leu Leu Ser Asn Asp  
 20 25 30

Leu Lys Leu Asn Leu Lys Met Arg Glu Glu Tyr Asp Lys Ile Gln Ile  
 35 40 45

Ala Asp Leu Met Glu Glu Lys Phe Arg Gly Asp Ala Gly Leu Gly Lys  
 50 55 60

Leu Ile Lys Ile Phe Glu Asp Ile Pro Thr Leu Glu Asp Leu Ala Glu  
 65 70 75 80

Thr Leu Lys Lys Glu Lys Leu Lys Val Lys Gly Pro Ala Leu Ser Arg  
 85 90 95

Lys Arg Lys Lys Glu Val His Ala Thr Ser Pro Ala Pro Ser Thr Ser  
 100 105 110

Ser Thr Val Lys Thr Glu Gly Ala Glu Ala Thr Pro Gly Ala Gln Lys  
 115 120 125

Arg Lys Lys Ser Thr Lys Glu Lys Ala Gly Pro Lys Gly Ser Lys Val  
 130 135 140

Ser Glu Glu Gln Thr Gln Pro Pro Ser Pro Ala Gly Ala Gly Met Ser  
 145 150 155 160

Thr Ala Met Gly Arg Ser Pro Ser Pro Lys Thr Ser Leu Ser Ala Pro  
 165 170 175

Pro Asn Ser Ser Ser Thr Glu Asn Pro Lys Thr Val Ala Lys Cys Gln  
 180 185 190

Val Thr Pro Arg Arg Asn Val Leu Gln Lys Arg Pro Val Ile Val Lys  
 195 200 205

Val Leu Ser Thr Thr Lys Pro Phe Glu Tyr Glu Thr Pro Glu Met Glu  
 210 215 220

Lys Lys Ile Met Phe His Ala Thr Val Ala Thr Gln Thr Gln Phe Phe  
 225 230 235 240

His Val Lys Val Leu Asn Thr Ser Leu Lys Glu Lys Phe Asn Gly Lys  
 245 250 255

Lys Ile Ile Ile Ile Ser Asp Tyr Leu Glu Tyr Asp Ser Leu Leu Glu  
 260 265 270  
 Val Asn Glu Glu Ser Thr Val Ser Glu Ala Gly Pro Asn Gln Thr Phe  
 275 280 285  
 Glu Val Pro Asn Lys Ile Ile Asn Arg Ala Lys Glu Thr Leu Lys Ile  
 290 295 300  
 Asp Ile Leu His Lys Gln Ala Ser Gly Asn Ile Val Tyr Gly Val Phe  
 305 310 315 320  
 Met Leu His Lys Lys Thr Val Asn Gln Lys Thr Thr Ile Tyr Glu Ile  
 325 330 335  
 Gln Asp Asp Arg Gly Lys Met Asp Val Val Gly Thr Gly Gln Cys His  
 340 345 350  
 Asn Ile Pro Cys Glu Glu Gly Asp Lys Leu Gln Leu Phe Cys Phe Arg  
 355 360 365  
 Leu Arg Lys Lys Asn Gln Met Ser Lys Leu Ile Ser Glu Met His Ser  
 370 375 380  
 Phe Ile Gln Ile Lys Lys Lys Thr Asn Pro Arg Asn Asn Asp Pro Lys  
 385 390 395 400  
 Ser Met Lys Leu Pro Gln Glu Gln Arg Gln Leu Pro Tyr Pro Ser Glu  
 405 410 415  
 Ala Ser Thr Thr Phe Pro Glu Ser His Leu Arg Thr Pro Gln Met Pro  
 420 425 430  
 Pro Thr Thr Pro Ser Ser Ser Phe Phe Thr Lys Lys Ser Glu Asp Thr  
 435 440 445  
 Ile Ser Lys Met Asn Asp Phe Met Arg Met Gln Ile Leu Lys Glu Gly  
 450 455 460  
 Ser His Phe Pro Gly Pro Phe Met Thr Ser Ile Gly Pro Ala Glu Ser  
 465 470 475 480  
 His Pro His Thr Pro Gln Met Pro Pro Ser Thr Pro Ser Ser Ser Phe  
 485 490 495  
 Leu Thr Thr Leu Lys Pro Arg Leu Lys Thr Glu Pro Glu Glu Val Ser  
 500 505 510  
 Ile Glu Asp Ser Ala Gln Ser Asp Leu Lys Glu Val Met Val Leu Asn  
 515 520 525  
 Ala Thr Glu Ser Phe Val Tyr Glu Pro Lys Glu Gln Lys Lys Met Phe  
 530 535 540  
 His Ala Thr Val Ala Thr Glu Asn Glu Val Phe Arg Val Lys Val Phe  
 545 550 555 560  
 Asn Ile Asp Leu Lys Glu Lys Phe Thr Pro Lys Lys Ile Ile Ala Ile  
 565 570 575

Ala Asn Tyr Val Cys Arg Asn Gly Phe Leu Glu Val Tyr Pro Phe Thr  
580 585 590

Leu Val Ala Asp Val Asn Ala Asp Arg Asn Met Glu Ile Pro Lys Gly  
595 600 605

Leu Ile Arg Ser Ala Ser Val Thr Pro Lys Ile Asn Gln Leu Cys Ser  
610 615 620

Gln Thr Lys Gly Ser Phe Val Asn Gly Val Phe Glu Val His Lys Lys  
625 630 635 640

Asn Val Arg Gly Glu Phe Thr Tyr Tyr Glu Ile Gln Asp Asn Thr Gly  
645 650 655

Lys Met Glu Val Val Val His Gly Arg Leu Asn Thr Ile Asn Cys Glu  
660 665 670

Glu Gly Asp Lys Leu Lys Leu Thr Ser Phe Glu Leu Ala Pro Lys Ser  
675 680 685

Gly Asn Thr Gly Glu Leu Arg Ser Val Ile His Ser His Ile Lys Val  
690 695 700

Ile Lys Thr Arg Lys Asn Lys Lys Asp Ile Leu Asn Pro Asp Ser Ser  
705 710 715 720

Met Glu Thr Ser Pro Asp Phe Phe Phe  
725

<210> 131  
<211> 216  
<212> PRT  
<213> Homo sapiens

<400> 131

Met Leu Arg Leu Ser Glu Arg Asn Met Lys Val Leu Leu Ala Ala Ala  
1 5 10 15

Leu Ile Ala Gly Ser Val Phe Phe Leu Leu Leu Pro Gly Pro Ser Ala  
20 25 30

Ala Asp Glu Lys Lys Lys Gly Pro Lys Val Thr Val Lys Val Tyr Phe  
35 40 45

Asp Leu Arg Ile Gly Asp Glu Asp Val Gly Arg Val Ile Phe Gly Leu  
50 55 60

Phe Gly Lys Thr Val Pro Lys Thr Val Asp Asn Phe Val Ala Leu Ala  
65 70 75 80

Thr Gly Glu Lys Gly Phe Gly Tyr Lys Asn Ser Lys Phe His Arg Val  
85 90 95

Ile Lys Asp Phe Met Ile Gln Gly Gly Asp Phe Thr Arg Gly Asp Gly  
100 105 110

Thr Gly Gly Lys Ser Ile Tyr Gly Glu Arg Phe Pro Asp Glu Asn Phe  
115 120 125

Lys Leu Lys His Tyr Gly Pro Gly Trp Val Ser Met Ala Asn Ala Gly  
130 135 140

Lys Asp Thr Asn Gly Ser Gln Phe Phe Ile Thr Thr Val Lys Thr Ala  
145 150 155 160

Trp Leu Asp Gly Lys His Val Val Phe Gly Lys Val Leu Glu Gly Met  
165 170 175

Glu Val Val Arg Lys Val Glu Ser Thr Lys Thr Asp Ser Arg Asp Lys  
180 185 190

Pro Leu Lys Asp Val Ile Ile Ala Asp Cys Gly Lys Ile Glu Val Glu  
195 200 205

Lys Pro Phe Ala Ile Ala Lys Glu  
210 215

<210> 132  
<211> 208  
<212> PRT  
<213> Homo sapiens

<400> 132

Met Lys Leu Leu Pro Ser Val Val Leu Lys Leu Phe Leu Ala Ala Val  
1 5 10 15

Leu Ser Ala Leu Val Thr Gly Glu Ser Leu Glu Arg Leu Arg Arg Gly  
20 25 30

Leu Ala Ala Gly Thr Ser Asn Pro Asp Pro Pro Thr Val Ser Thr Asp  
35 40 45

Gln Leu Leu Pro Leu Gly Gly Gly Arg Asp Arg Lys Val Arg Asp Leu  
50 55 60

Gln Glu Ala Asp Leu Asp Leu Leu Arg Val Thr Leu Ser Ser Lys Pro  
65 70 75 80

Gln Ala Leu Ala Thr Pro Asn Lys Glu Glu His Gly Lys Arg Lys Lys  
85 90 95

Lys Gly Lys Gly Leu Gly Lys Lys Arg Asp Pro Cys Leu Arg Lys Tyr  
100 105 110

Lys Asp Phe Cys Ile His Gly Glu Cys Lys Tyr Val Lys Glu Leu Arg  
115 120 125

Ala Pro Ser Cys Ile Cys His Pro Gly Tyr His Gly Glu Arg Cys His  
130 135 140

Gly Leu Ser Leu Pro Val Glu Asn Arg Leu Tyr Thr Tyr Asp His Thr  
145 150 155 160

Thr Ile Leu Ala Val Val Ala Val Val Leu Ser Ser Val Cys Leu Leu  
165 170 175

Val Ile Val Gly Leu Leu Met Phe Arg Tyr His Arg Arg Gly Gly Tyr  
180 185 190

Asp Val Glu Asn Glu Glu Lys Val Lys Leu Gly Met Thr Asn Ser His  
 195 200 205

<210> 133  
 <211> 178  
 <212> PRT  
 <213> Homo sapiens

<400> 133

Met Thr Thr Leu Arg Ala Phe Thr Cys Asp Asp Leu Phe Arg Phe Asn  
 1 5 10 15

Asn Ile Asn Leu Asp Pro Leu Thr Glu Thr Tyr Gly Ile Pro Phe Tyr  
 20 25 30

Leu Gln Tyr Leu Ala His Trp Pro Glu Tyr Phe Ile Val Ala Glu Ala  
 35 40 45

Pro Gly Gly Glu Leu Met Gly Tyr Ile Met Gly Lys Ala Glu Gly Ser  
 50 55 60

Val Ala Arg Glu Glu Trp His Gly His Val Thr Ala Leu Ser Val Ala  
 65 70 75 80

Pro Glu Phe Arg Arg Leu Gly Leu Ala Ala Lys Leu Met Glu Leu Leu  
 85 90 95

Glu Glu Ile Ser Glu Arg Lys Gly Gly Phe Phe Val Asp Leu Phe Val  
 100 105 110

Arg Val Ser Asn Gln Val Ala Val Asn Met Tyr Lys Gln Leu Gly Tyr  
 115 120 125

Ser Val Tyr Arg Thr Val Ile Glu Tyr Tyr Ser Ala Ser Asn Gly Glu  
 130 135 140

Pro Asp Glu Asp Ala Tyr Asp Met Arg Lys Ala Leu Ser Arg Asp Thr  
 145 150 155 160

Glu Lys Lys Ser Ile Ile Pro Leu Pro His Pro Val Arg Pro Glu Asp  
 165 170 175

Ile Glu

<210> 134  
 <211> 185  
 <212> PRT  
 <213> Homo sapiens

<400> 134

Met Gly Pro Glu Arg His Leu Ser Gly Ala Pro Ala Arg Met Ala Thr  
 1 5 10 15

Val Val Leu Gly Gly Asp Thr Met Gly Pro Glu Arg Ile Phe Pro Asn  
 20 25 30

Gln Thr Glu Glu Leu Gly His Gln Gly Pro Ser Glu Gly Thr Gly Asp  
 35 40 45

Trp Ser Ser Glu Glu Pro Glu Glu Glu Gln Glu Glu Thr Gly Ser Gly  
50 55 60

Pro Ala Gly Tyr Ser Tyr Gln Pro Leu Asn Gln Asp Pro Glu Gln Glu  
65 70 75 80

Glu Val Glu Leu Ala Pro Val Gly Asp Gly Asp Val Val Ala Asp Ile  
85 90 95

Gln Asp Arg Ile Gln Ala Leu Gly Leu His Leu Pro Asp Pro Pro Leu  
100 105 110

Glu Ser Glu Asp Glu Asp Glu Glu Gly Ala Thr Ala Leu Asn Asn His  
115 120 125

Ser Ser Ile Pro Met Asp Pro Glu His Val Glu Leu Val Lys Arg Thr  
130 135 140

Met Ala Gly Val Ser Leu Pro Ala Pro Gly Val Pro Ala Trp Ala Arg  
145 150 155 160

Glu Ile Ser Asp Ala Gln Trp Glu Asp Val Val Gln Lys Ala Leu Gln  
165 170 175

Ala Arg Gln Ala Ser Pro Ala Trp Lys  
180 185

<210> 135  
<211> 397  
<212> PRT  
<213> Homo sapiens

<400> 135

Met Asn Ala Gly Ser Asp Pro Val Val Ile Val Ser Ala Ala Arg Thr  
1 5 10 15

Ile Ile Gly Ser Phe Asn Gly Ala Leu Ala Ala Val Pro Val Gln Asp  
20 25 30

Leu Gly Ser Thr Val Ile Lys Glu Val Leu Lys Arg Ala Thr Val Ala  
35 40 45

Pro Glu Asp Val Ser Glu Val Ile Phe Gly His Val Leu Ala Ala Gly  
50 55 60

Cys Gly Gln Asn Pro Val Arg Gln Ala Ser Val Gly Ala Gly Ile Pro  
65 70 75 80

Tyr Ser Val Pro Ala Trp Ser Cys Gln Met Ile Cys Gly Ser Gly Leu  
85 90 95

Lys Ala Val Cys Leu Ala Val Gln Ser Ile Gly Ile Gly Asp Ser Ser  
100 105 110

Ile Val Val Ala Gly Gly Met Glu Asn Met Ser Lys Ala Pro His Leu  
115 120 125

Ala Tyr Leu Arg Thr Gly Val Lys Ile Gly Glu Met Pro Leu Thr Asp  
130 135 140

Ser Ile Leu Cys Asp Gly Leu Thr Asp Ala Phe His Asn Cys His Met  
 145 150 155 160  
 Gly Ile Thr Ala Glu Asn Val Ala Thr Lys Trp Gln Val Ser Arg Glu  
 165 170 175  
 Asp Gln Asp Lys Val Ala Val Leu Ser Gln Asn Arg Thr Glu Asn Ala  
 180 185 190  
 Gln Lys Ala Gly His Phe Asp Lys Glu Ile Val Pro Val Leu Val Ser  
 195 200 205  
 Thr Arg Lys Gly Leu Ile Glu Val Lys Thr Asp Glu Phe Pro Arg His  
 210 215 220  
 Gly Ser Asn Ile Glu Ala Met Ser Lys Leu Lys Pro Tyr Phe Leu Thr  
 225 230 235 240  
 Asp Gly Thr Gly Thr Val Thr Pro Ala Asn Ala Ser Gly Ile Asn Asp  
 245 250 255  
 Gly Ala Ala Ala Val Ala Leu Met Lys Lys Ser Glu Ala Asp Lys Arg  
 260 265 270  
 Gly Leu Thr Pro Leu Ala Arg Ile Val Ser Trp Ser Gln Val Gly Val  
 275 280 285  
 Glu Pro Ser Ile Met Gly Ile Gly Pro Ile Pro Ala Ile Lys Gln Ala  
 290 295 300  
 Val Thr Lys Ala Gly Trp Ser Leu Glu Asp Val Asp Ile Phe Glu Ile  
 305 310 315 320  
 Asn Glu Ala Phe Ala Ala Val Ser Ala Ala Ile Val Lys Glu Leu Gly  
 325 330 335  
 Leu Asn Pro Glu Lys Val Asn Ile Glu Gly Gly Ala Ile Ala Leu Gly  
 340 345 350  
 His Pro Leu Gly Ala Ser Gly Cys Arg Ile Leu Val Thr Leu Leu His  
 355 360 365  
 Thr Leu Glu Arg Met Gly Arg Ser Arg Gly Val Ala Ala Leu Cys Ile  
 370 375 380  
 Gly Gly Gly Met Gly Ile Ala Met Cys Val Gln Arg Glu  
 385 390 395  
 <210> 136  
 <211> 556  
 <212> PRT  
 <213> Homo sapiens  
 <400> 136  
 Met Glu Gly Pro Leu Ser Val Phe Gly Asp Arg Ser Thr Gly Glu Thr  
 1 5 10 15  
 Ile Arg Ser Gln Asn Val Met Ala Ala Ala Ser Ile Ala Asn Ile Val  
 20 25 30



Lys Ser Ser Leu Gly Pro Val Gly Leu Asp Lys Met Leu Val Asp Asp  
 35 40 45  
 Ile Gly Asp Val Thr Ile Thr Asn Asp Gly Ala Thr Ile Leu Lys Leu  
 50 55 60  
 Leu Glu Val Glu His Pro Ala Ala Lys Val Leu Cys Glu Leu Ala Asp  
 65 70 75 80  
 Leu Gln Asp Lys Glu Val Gly Asp Gly Thr Thr Ser Val Val Ile Ile  
 85 90 95  
 Ala Ala Glu Leu Leu Lys Asn Ala Asp Glu Leu Val Lys Gln Lys Ile  
 100 105 110  
 His Pro Thr Ser Val Ile Ser Gly Tyr Arg Leu Ala Cys Lys Glu Ala  
 115 120 125  
 Val Arg Tyr Ile Asn Glu Asn Leu Ile Val Asn Thr Asp Glu Leu Gly  
 130 135 140  
 Arg Asp Cys Leu Ile Asn Ala Ala Lys Thr Ser Met Ser Ser Lys Ile  
 145 150 155 160  
 Ile Gly Ile Asn Gly Asp Phe Phe Ala Asn Met Val Val Asp Ala Val  
 165 170 175  
 Leu Ala Ile Lys Tyr Thr Asp Ile Arg Gly Gln Pro Arg Tyr Pro Val  
 180 185 190  
 Asn Ser Val Asn Ile Leu Lys Ala His Gly Arg Ser Gln Met Glu Ser  
 195 200 205  
 Met Leu Ile Ser Gly Tyr Ala Leu Asn Cys Val Val Gly Ser Gln Gly  
 210 215 220  
 Met Pro Lys Arg Ile Val Asn Ala Lys Ile Ala Cys Leu Asp Phe Ser  
 225 230 235 240  
 Leu Gln Lys Thr Lys Met Lys Leu Gly Val Gln Val Val Ile Thr Asp  
 245 250 255  
 Pro Glu Lys Leu Asp Gln Ile Arg Gln Arg Glu Ser Asp Ile Thr Lys  
 260 265 270  
 Glu Arg Ile Gln Lys Ile Leu Ala Thr Gly Ala Asn Val Ile Leu Thr  
 275 280 285  
 Thr Gly Gly Ile Asp Asp Met Cys Leu Lys Tyr Phe Val Glu Ala Gly  
 290 295 300  
 Ala Met Ala Val Arg Arg Val Leu Lys Arg Asp Leu Lys Arg Ile Ala  
 305 310 315 320  
 Lys Ala Ser Gly Ala Thr Ile Leu Ser Thr Leu Ala Asn Leu Glu Gly  
 325 330 335  
 Glu Glu Thr Phe Glu Ala Ala Met Leu Gly Gln Ala Glu Glu Val Val  
 340 345 350

Gln Glu Arg Ile Cys Asp Asp Glu Leu Ile Leu Ile Lys Asn Thr Lys  
355 360 365

Ala Arg Thr Ser Ala Ser Ile Ile Leu Arg Gly Ala Asn Asp Phe Met  
370 375 380

Cys Asp Glu Met Glu Arg Ser Leu His Asp Ala Leu Cys Val Val Lys  
385 390 395 400

Arg Val Leu Glu Ser Lys Ser Val Val Pro Gly Gly Gly Ala Val Glu  
405 410 415

Ala Ala Leu Ser Ile Tyr Leu Glu Asn Tyr Ala Thr Ser Met Gly Ser  
420 425 430

Arg Glu Gln Leu Ala Ile Ala Glu Phe Ala Arg Ser Leu Leu Val Ile  
435 440 445

Pro Asn Thr Leu Ala Val Asn Ala Ala Gln Asp Ser Thr Asp Leu Val  
450 455 460

Ala Lys Leu Arg Ala Phe His Asn Glu Ala Gln Val Asn Pro Glu Arg  
465 470 475 480

Lys Asn Leu Lys Trp Ile Gly Leu Asp Leu Ser Asn Gly Lys Pro Arg  
485 490 495

Asp Asn Lys Gln Ala Gly Val Phe Glu Pro Thr Ile Val Lys Val Lys  
500 505 510

Ser Leu Lys Phe Ala Thr Glu Ala Ala Ile Thr Ile Leu Arg Ile Asp  
515 520 525

Asp Leu Ile Lys Leu His Pro Glu Ile Leu Arg Ile Lys His Gly Ser  
530 535 540

Tyr Glu Asp Ala Val His Ser Gly Ala Leu Asn Asp  
545 550 555

<210> 137

<211> 266

<212> PRT

<213> Homo sapiens

<400> 137

Met Pro Lys Gly Lys Lys Ala Lys Gly Lys Lys Val Ala Pro Ala Pro  
1 5 10 15

Ala Val Val Lys Lys Gln Glu Ala Lys Lys Val Val Asn Pro Leu Phe  
20 25 30

Glu Lys Arg Pro Lys Asn Phe Gly Ile Gly Gln Asp Ile Gln Pro Lys  
35 40 45

Arg Asp Leu Thr Arg Phe Val Lys Trp Pro Arg Tyr Ile Arg Leu Gln  
50 55 60

Arg Gln Arg Ala Ile Leu Tyr Lys Arg Leu Lys Val Pro Pro Ala Ile  
65 70 75 80

Asn Gln Phe Thr Gln Ala Leu Asp Arg Gln Thr Ala Thr Gln Leu Leu  
85 90 95

Lys Leu Ala His Lys Tyr Arg Pro Glu Thr Lys Gln Glu Lys Lys Gln  
100 105 110

Arg Leu Leu Ala Arg Ala Glu Lys Lys Ala Ala Gly Lys Gly Asp Val  
115 120 125

Pro Thr Lys Arg Pro Pro Val Leu Arg Ala Gly Val Asn Thr Val Thr  
130 135 140

Thr Leu Val Glu Asn Lys Lys Ala Gln Leu Val Val Ile Ala His Asp  
145 150 155 160

Val Asp Pro Ile Glu Leu Val Val Phe Leu Pro Ala Leu Cys Arg Lys  
165 170 175

Met Gly Val Pro Tyr Cys Ile Ile Lys Gly Lys Ala Arg Leu Gly Arg  
180 185 190

Leu Val His Arg Lys Thr Cys Thr Thr Val Ala Phe Thr Gln Val Asn  
195 200 205

Ser Glu Asp Lys Gly Ala Leu Ala Lys Leu Val Glu Ala Ile Arg Thr  
210 215 220

Asn Tyr Asn Asp Arg Tyr Asp Glu Ile Arg Arg His Trp Gly Gly Asn  
225 230 235 240

Val Leu Gly Pro Lys Ser Val Ala Arg Ile Ala Lys Leu Glu Lys Ala  
245 250 255

Lys Ala Lys Glu Leu Ala Thr Lys Leu Gly  
260 265

<210> 138  
<211> 160  
<212> PRT  
<213> Homo sapiens

<400> 138

Met Asp Cys Gln Asn Gly His Gln His Ile Ser Gln Glu Leu Glu Val  
1 5 10 15

Leu Arg Ile His Met Gln Leu Val Thr Val Gln Phe Thr Gln Leu Gly  
20 25 30

Lys Gly Ala Leu Glu Ile Ile Gln Val Leu Cys Gly Ile Ser Gln Gly  
35 40 45

Ser Gln His Leu Leu Ala Met Cys Leu Asp Phe Gly Val Ala His Asp  
50 55 60

Gly Arg Gly Arg Gly Gln Val Ala Lys Ala Val Lys Glu Pro Leu Gly  
65 70 75 80

Pro Trp Val Asp Asn Gln Glu Pro Ser Gln Gly Phe Ser Ser Ser Ile  
85 90 95

Phe His Ile His Leu Ala Pro Gln Ala Cys Asp Ser Ser Leu Val Leu  
 100 105 110

Leu Cys Glu Met Thr His Gly Val Trp Thr Arg Ser Leu Leu Ile Thr  
 115 120 125

Ser Asp Val Pro Glu Ala Ser Val Thr Gln Ile Leu Leu Cys Ala Met  
 130 135 140

Trp Thr Leu Pro Ser His Ala Thr Thr Arg Glu Leu Thr Gln Trp Val  
 145 150 155 160

<210> 139  
 <211> 172  
 <212> PRT  
 <213> Homo sapiens

<400> 139

Met Ile Ile Tyr Arg Asp Leu Ile Ser His Asp Glu Met Phe Ser Asp  
 1 5 10 15

Ile Tyr Lys Ile Arg Glu Ile Ala Asp Gly Leu Cys Leu Glu Val Glu  
 20 25 30

Gly Lys Met Val Ser Arg Thr Glu Gly Asn Ile Asp Asp Ser Leu Ile  
 35 40 45

Gly Gly Asn Ala Ser Ala Glu Gly Pro Glu Gly Glu Gly Thr Glu Ser  
 50 55 60

Thr Val Ile Thr Gly Val Asp Ile Val Met Asn His His Leu Gln Glu  
 65 70 75 80

Thr Ser Phe Thr Lys Glu Ala Tyr Lys Lys Tyr Ile Lys Asp Tyr Met  
 85 90 95

Lys Ser Ile Lys Gly Lys Leu Glu Glu Gln Arg Pro Glu Arg Val Lys  
 100 105 110

Pro Phe Met Thr Gly Ala Ala Glu Gln Ile Lys His Ile Leu Ala Asn  
 115 120 125

Phe Lys Asn Tyr Gln Phe Phe Ile Gly Glu Asn Met Asn Pro Asp Gly  
 130 135 140

Met Val Ala Leu Leu Asp Tyr Arg Glu Asp Gly Val Thr Pro Tyr Met  
 145 150 155 160

Ile Phe Phe Lys Asp Gly Leu Glu Met Glu Lys Cys  
 165 170

<210> 140  
 <211> 133  
 <212> PRT  
 <213> Homo sapiens

<400> 140

Met Asn Asp Thr Val Thr Ile Arg Thr Arg Lys Phe Met Thr Asn Arg  
 1 5 10 15

Leu Leu Gln Arg Lys Gln Met Val Ile Asp Val Leu His Pro Gly Lys  
                   20                                  25                                  30

Ala Thr Val Pro Lys Thr Glu Ile Arg Glu Lys Leu Ala Lys Met Tyr  
                   35                                  40                                  45

Lys Thr Thr Pro Asp Val Ile Phe Val Phe Gly Phe Arg Thr His Phe  
                   50                                  55                                  60

Gly Gly Gly Lys Thr Thr Gly Phe Gly Met Ile Tyr Asp Ser Leu Asp  
   65                                  70                                  75                                  80

Tyr Ala Lys Lys Asn Glu Pro Lys His Arg Leu Ala Arg His Gly Leu  
                   85                                  90                                  95

Tyr Glu Lys Lys Lys Thr Ser Arg Lys Gln Arg Lys Glu Arg Lys Asn  
                   100                                  105                                  110

Arg Met Lys Lys Val Arg Gly Thr Ala Lys Ala Asn Val Gly Ala Gly  
                   115                                  120                                  125

Lys Lys Pro Lys Glu  
                   130

<210> 141  
 <211> 604  
 <212> PRT  
 <213> Homo sapiens

<400> 141

Met Asn Ile Val Glu Asn Ser Ile Phe Leu Ser Asn Leu Met Lys Ser  
   1                  5                                  10                                  15

Ala Tyr Thr Phe Glu Leu Lys Tyr Asp Leu Ser Cys Glu Leu Tyr Arg  
                   20                                  25                                  30

Met Ser Thr Tyr Ser Thr Phe Pro Ala Gly Val Pro Val Ser Glu Arg  
                   35                                  40                                  45

Ser Leu Ala Arg Ala Gly Phe Tyr Tyr Thr Gly Val Asn Asp Lys Val  
                   50                                  55                                  60

Lys Cys Phe Cys Cys Gly Leu Met Leu Asp Asn Trp Lys Arg Gly Asp  
   65                                  70                                  75                                  80

Ser Pro Thr Glu Lys His Lys Lys Leu Tyr Pro Ser Cys Arg Phe Val  
                   85                                  90                                  95

Gln Ser Leu Asn Ser Val Asn Asn Leu Glu Ala Thr Ser Gln Pro Thr  
                   100                                  105                                  110

Phe Pro Ser Ser Val Thr Asn Ser Thr His Ser Leu Leu Pro Gly Thr  
                   115                                  120                                  125

Glu Asn Ser Gly Tyr Phe Arg Gly Ser Tyr Ser Asn Ser Pro Ser Asn  
   130                                  135                                  140

Pro Val Asn Ser Arg Ala Asn Gln Asp Phe Ser Ala Leu Met Arg Ser  
   145                                  150                                  155                                  160

Ser Tyr His Cys Ala Met Asn Asn Glu Asn Ala Arg Leu Leu Thr Phe  
 165 170 175  
 Gln Thr Trp Pro Leu Thr Phe Leu Ser Pro Thr Asp Leu Ala Lys Ala  
 180 185 190  
 Gly Phe Tyr Tyr Ile Gly Pro Gly Asp Arg Val Ala Cys Phe Ala Cys  
 195 200 205  
 Gly Gly Lys Leu Ser Asn Trp Glu Pro Lys Asp Asn Ala Met Ser Glu  
 210 215 220  
 His Leu Arg His Phe Pro Lys Cys Pro Phe Ile Glu Asn Gln Leu Gln  
 225 230 235 240  
 Asp Thr Ser Arg Tyr Thr Val Ser Asn Leu Ser Met Gln Thr His Ala  
 245 250 255  
 Ala Arg Phe Lys Thr Phe Phe Asn Trp Pro Ser Ser Val Leu Val Asn  
 260 265 270  
 Pro Glu Gln Leu Ala Ser Ala Gly Phe Tyr Tyr Val Gly Asn Ser Asp  
 275 280 285  
 Asp Val Lys Cys Phe Cys Cys Asp Gly Gly Leu Arg Cys Trp Glu Ser  
 290 295 300  
 Gly Asp Asp Pro Trp Val Gln His Ala Lys Trp Phe Pro Arg Cys Glu  
 305 310 315 320  
 Tyr Leu Ile Arg Ile Lys Gly Gln Glu Phe Ile Arg Gln Val Gln Ala  
 325 330 335  
 Ser Tyr Pro His Leu Leu Glu Gln Leu Leu Ser Thr Ser Asp Ser Pro  
 340 345 350  
 Gly Asp Glu Asn Ala Glu Ser Ser Ile Ile His Phe Glu Pro Gly Glu  
 355 360 365  
 Asp His Ser Glu Asp Ala Ile Met Met Asn Thr Pro Val Ile Asn Ala  
 370 375 380  
 Ala Val Glu Met Gly Phe Ser Arg Ser Leu Val Lys Gln Thr Val Gln  
 385 390 395 400  
 Arg Lys Ile Leu Ala Thr Gly Glu Asn Tyr Arg Leu Val Asn Asp Leu  
 405 410 415  
 Val Leu Asp Leu Leu Asn Ala Glu Asp Glu Ile Arg Glu Glu Glu Arg  
 420 425 430  
 Glu Arg Ala Thr Glu Glu Lys Glu Ser Asn Asp Leu Leu Leu Ile Arg  
 435 440 445  
 Lys Asn Arg Met Ala Leu Phe Gln His Leu Thr Cys Val Ile Pro Ile  
 450 455 460  
 Leu Asp Ser Leu Leu Thr Ala Gly Ile Ile Asn Glu Gln Glu His Asp  
 465 470 475 480

Val Ile Lys Gln Lys Thr Gln Thr Ser Leu Gln Ala Arg Glu Leu Ile  
485 490 495

Asp Thr Ile Leu Val Lys Gly Asn Ile Ala Ala Thr Val Phe Arg Asn  
500 505 510

Ser Leu Gln Glu Ala Glu Ala Val Leu Tyr Glu His Leu Phe Val Gln  
515 520 525

Gln Asp Ile Lys Tyr Ile Pro Thr Glu Asp Val Ser Asp Leu Pro Val  
530 535 540

Glu Glu Gln Leu Arg Arg Leu Gln Glu Glu Arg Thr Cys Lys Val Cys  
545 550 555 560

Met Asp Lys Glu Val Ser Ile Val Phe Ile Pro Cys Gly His Leu Val  
565 570 575

Val Cys Lys Asp Cys Ala Pro Ser Leu Arg Lys Cys Pro Ile Cys Arg  
580 585 590

Ser Thr Ile Lys Gly Thr Val Arg Thr Phe Leu Ser  
595 600

<210> 142  
<211> 624  
<212> PRT  
<213> Homo sapiens

<400> 142

Met Gln Pro Asp Pro Arg Pro Ser Gly Ala Gly Ala Cys Cys Arg Phe  
1 5 10 15

Leu Pro Leu Gln Ser Gln Cys Pro Glu Gly Ala Gly Asp Ala Val Met  
20 25 30

Tyr Ala Ser Thr Glu Cys Lys Ala Glu Val Thr Pro Ser Gln His Gly  
35 40 45

Asn Arg Thr Phe Ser Tyr Thr Leu Glu Asp His Thr Lys Gln Ala Phe  
50 55 60

Gly Ile Met Asn Glu Leu Arg Leu Ser Gln Gln Leu Cys Asp Val Thr  
65 70 75 80

Leu Gln Val Lys Tyr Gln Asp Ala Pro Ala Ala Gln Phe Met Ala His  
85 90 95

Lys Val Val Leu Ala Ser Ser Ser Pro Val Phe Lys Ala Met Phe Thr  
100 105 110

Asn Gly Leu Arg Glu Gln Gly Met Glu Val Val Ser Ile Glu Gly Ile  
115 120 125

His Pro Lys Val Met Glu Arg Leu Ile Glu Phe Ala Tyr Thr Ala Ser  
130 135 140

Ile Ser Met Gly Glu Lys Cys Val Leu His Val Met Asn Gly Ala Val  
145 150 155 160

Met Tyr Gln Ile Asp Ser Val Val Arg Ala Cys Ser Asp Phe Leu Val  
 165 170 175  
 Gln Gln Leu Asp Pro Ser Asn Ala Ile Gly Ile Ala Asn Phe Ala Glu  
 180 185 190  
 Gln Ile Gly Cys Val Glu Leu His Gln Arg Ala Arg Glu Tyr Ile Tyr  
 195 200 205  
 Met His Phe Gly Glu Val Ala Lys Gln Glu Glu Phe Phe Asn Leu Ser  
 210 215 220  
 His Cys Gln Leu Val Thr Leu Ile Ser Arg Asp Asp Leu Asn Val Arg  
 225 230 235 240  
 Cys Glu Ser Glu Val Phe His Ala Cys Ile Asn Trp Val Lys Tyr Asp  
 245 250 255  
 Cys Glu Gln Arg Arg Phe Tyr Val Gln Ala Leu Leu Arg Ala Val Arg  
 260 265 270  
 Cys His Ser Leu Thr Pro Asn Phe Leu Gln Met Gln Leu Gln Lys Cys  
 275 280 285  
 Glu Ile Leu Gln Ser Asp Ser Arg Cys Lys Asp Tyr Leu Val Lys Ile  
 290 295 300  
 Phe Glu Glu Leu Thr Leu His Lys Pro Thr Gln Val Met Pro Cys Arg  
 305 310 315 320  
 Ala Pro Lys Val Gly Arg Leu Ile Tyr Thr Ala Gly Gly Tyr Phe Arg  
 325 330 335  
 Gln Ser Leu Ser Tyr Leu Glu Ala Tyr Asn Pro Ser Asn Gly Thr Trp  
 340 345 350  
 Leu Arg Leu Ala Asp Leu Gln Val Pro Arg Ser Gly Leu Ala Gly Cys  
 355 360 365  
 Val Val Gly Gly Leu Leu Tyr Ala Val Gly Gly Arg Asn Asn Ser Pro  
 370 375 380  
 Asp Gly Asn Thr Asp Ser Ser Ala Leu Asp Cys Tyr Asn Pro Met Thr  
 385 390 395 400  
 Asn Gln Trp Ser Pro Cys Ala Pro Met Ser Val Pro Arg Asn Arg Ile  
 405 410 415  
 Gly Val Gly Val Ile Asp Gly His Ile Tyr Ala Val Gly Gly Ser His  
 420 425 430  
 Gly Cys Ile His His Asn Ser Val Glu Arg Tyr Glu Pro Glu Arg Asp  
 435 440 445  
 Glu Trp His Leu Val Ala Pro Met Leu Thr Arg Arg Ile Gly Val Gly  
 450 455 460  
 Val Ala Val Leu Asn Arg Leu Leu Tyr Ala Val Gly Gly Phe Asp Gly  
 465 470 475 480



Thr Asn Arg Leu Asn Ser Ala Glu Cys Tyr Tyr Pro Glu Arg Asn Glu  
485 490 495

Trp Arg Met Ile Thr Ala Met Asn Thr Ile Arg Ser Gly Ala Gly Val  
500 505 510

Cys Val Leu His Asn Cys Ile Tyr Ala Ala Gly Gly Tyr Asp Gly Gln  
515 520 525

Asp Gln Leu Asn Ser Val Glu Arg Tyr Asp Val Glu Thr Glu Thr Trp  
530 535 540

Thr Phe Val Ala Pro Met Lys His Arg Arg Ser Ala Leu Gly Ile Thr  
545 550 555 560

Val His Gln Gly Arg Ile Tyr Val Leu Gly Gly Tyr Asp Gly His Thr  
565 570 575

Phe Leu Asp Ser Val Glu Cys Tyr Asp Pro Asp Thr Asp Thr Trp Ser  
580 585 590

Glu Val Thr Arg Met Thr Ser Gly Arg Ser Gly Val Gly Val Ala Val  
595 600 605

Thr Met Glu Pro Cys Arg Lys Gln Ile Asp Gln Gln Asn Cys Thr Cys  
610 615 620

<210> 143  
<211> 389  
<212> PRT  
<213> Homo sapiens

<400> 143

Met Leu Ser Leu Arg Val Pro Leu Ala Pro Ile Thr Asp Pro Gln Gln  
1 5 10 15

Leu Gln Leu Ser Pro Leu Lys Gly Leu Ser Leu Val Asp Lys Glu Asn  
20 25 30

Thr Pro Pro Ala Leu Ser Gly Thr Arg Val Leu Ala Ser Lys Thr Ala  
35 40 45

Arg Arg Ile Phe Gln Glu Pro Thr Glu Pro Lys Thr Lys Ala Ala Ala  
50 55 60

Pro Gly Val Glu Asp Glu Pro Leu Leu Arg Glu Asn Pro Arg Arg Phe  
65 70 75 80

Val Ile Phe Pro Ile Glu Tyr His Asp Ile Trp Gln Met Tyr Lys Lys  
85 90 95

Ala Glu Ala Ser Phe Trp Thr Ala Glu Glu Val Asp Leu Ser Lys Asp  
100 105 110

Ile Gln His Trp Glu Ser Leu Lys Pro Glu Glu Arg Tyr Phe Ile Ser  
115 120 125

His Val Leu Ala Phe Phe Ala Ala Ser Asp Gly Ile Val Asn Glu Asn  
130 135 140

Leu Val Glu Arg Phe Ser Gln Glu Val Gln Ile Thr Glu Ala Arg Cys  
 145 150 155 160  
 Phe Tyr Gly Phe Gln Ile Ala Met Glu Asn Ile His Ser Glu Met Tyr  
 165 170 175  
 Ser Leu Leu Ile Asp Thr Tyr Ile Lys Asp Pro Lys Glu Arg Glu Phe  
 180 185 190  
 Leu Phe Asn Ala Ile Glu Thr Met Pro Cys Val Lys Lys Lys Ala Asp  
 195 200 205  
 Trp Ala Leu Arg Trp Ile Gly Asp Lys Glu Ala Thr Tyr Gly Glu Arg  
 210 215 220  
 Val Val Ala Phe Ala Ala Val Glu Gly Ile Phe Phe Ser Gly Ser Phe  
 225 230 235 240  
 Ala Ser Ile Phe Trp Leu Lys Lys Arg Gly Leu Met Pro Gly Leu Thr  
 245 250 255  
 Phe Ser Asn Glu Leu Ile Ser Arg Asp Glu Gly Leu His Cys Asp Phe  
 260 265 270  
 Ala Cys Leu Met Phe Lys His Leu Val His Lys Pro Ser Glu Glu Arg  
 275 280 285  
 Val Arg Glu Ile Ile Ile Asn Ala Val Arg Ile Glu Gln Glu Phe Leu  
 290 295 300  
 Thr Glu Ala Leu Pro Val Lys Leu Ile Gly Met Asn Cys Thr Leu Met  
 305 310 315 320  
 Lys Gln Tyr Ile Glu Phe Val Ala Asp Arg Leu Met Leu Glu Leu Gly  
 325 330 335  
 Phe Ser Lys Val Phe Arg Val Glu Asn Pro Phe Asp Phe Met Glu Asn  
 340 345 350  
 Ile Ser Leu Glu Gly Lys Thr Asn Phe Phe Glu Lys Arg Val Gly Glu  
 355 360 365  
 Tyr Gln Arg Met Gly Val Met Ser Ser Pro Thr Glu Asn Ser Phe Thr  
 370 375 380  
 Leu Asp Ala Asp Phe  
 385  
 <210> 144  
 <211> 281  
 <212> PRT  
 <213> Homo sapiens  
 <400> 144  
 Met Ala Thr Asn Phe Leu Ala His Glu Lys Ile Trp Phe Asp Lys Phe  
 1 5 10 15  
 Lys Tyr Asp Asp Ala Glu Arg Arg Phe Tyr Glu Gln Met Asn Gly Pro  
 20 25 30

Val Arg Gly Ala Ser Arg Gln Glu Asn Gly Ala Thr Val Ile Leu Arg  
 35 40 45  
 Asp Ile Ala Arg Ala Arg Glu Asn Ile Gln Lys Ser Leu Ala Gly Ser  
 50 55 60  
 Ser Gly Pro Gly Ala Ser Ser Gly Thr Ser Gly Asp His Gly Glu Leu  
 65 70 75 80  
 Val Val Arg Ile Ala Ser Leu Glu Val Glu Asn Gln Ser Leu Arg Gly  
 85 90 95  
 Val Val Gln Glu Leu Gln Gln Ala Ile Ser Lys Leu Glu Ala Arg Leu  
 100 105 110  
 Asn Val Leu Glu Lys Ser Ser Pro Gly His Arg Ala Thr Ala Pro Gln  
 115 120 125  
 Thr Gln His Val Ser Pro Met Arg Gln Val Glu Pro Pro Ala Lys Lys  
 130 135 140  
 Pro Ala Thr Pro Ala Glu Asp Asp Glu Asp Asp Asp Ile Asp Leu Phe  
 145 150 155 160  
 Gly Ser Asp Asn Glu Glu Glu Asp Lys Glu Ala Ala Gln Leu Arg Glu  
 165 170 175  
 Glu Arg Leu Arg Gln Tyr Ala Glu Lys Lys Ala Lys Lys Pro Ala Leu  
 180 185 190  
 Val Ala Lys Ser Ser Ile Leu Leu Asp Val Lys Pro Trp Asp Asp Glu  
 195 200 205  
 Thr Asp Met Ala Gln Leu Glu Ala Cys Val Arg Ser Ile Gln Leu Asp  
 210 215 220  
 Gly Leu Val Trp Gly Ala Ser Lys Leu Val Pro Val Gly Tyr Gly Ile  
 225 230 235 240  
 Arg Lys Leu Gln Ile Gln Cys Val Val Glu Asp Asp Lys Val Gly Thr  
 245 250 255  
 Asp Leu Leu Glu Glu Glu Ile Thr Lys Phe Glu Glu His Val Gln Ser  
 260 265 270  
 Val Asp Ile Ala Ala Phe Asn Lys Ile  
 275 280

<210> 145  
 <211> 269  
 <212> PRT  
 <213> Homo sapiens

<400> 145

Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp  
 1 5 10 15

Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His  
 20 25 30

Leu Val Leu Arg Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu  
 35 40 45  
 Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile Glu  
 50 55 60  
 Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln  
 65 70 75 80  
 Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu  
 85 90 95  
 Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu Arg  
 100 105 110  
 Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr  
 115 120 125  
 Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala  
 130 135 140  
 Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile  
 145 150 155 160  
 Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn  
 165 170 175  
 Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly  
 180 185 190  
 Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu  
 195 200 205  
 Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp  
 210 215 220  
 Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys  
 225 230 235 240  
 Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu  
 245 250 255  
 Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Val  
 260 265

<210> 146  
 <211> 1231  
 <212> PRT  
 <213> Homo sapiens

<400> 146

Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys  
 1 5 10 15

Val Ala Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn Thr Glu Ile  
 20 25 30

Leu Thr Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly Thr Gln Ala  
 35 40 45

Ile Tyr Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Val Ile Met  
 50 55 60  
 Val Cys Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys Cys  
 65 70 75 80  
 Gln Lys Arg Pro Cys Gly His Pro Gly Asp Thr Pro Phe Gly Thr Phe  
 85 90 95  
 Thr Leu Thr Gly Gly Asn Val Phe Glu Tyr Gly Val Lys Ala Val Tyr  
 100 105 110  
 Thr Cys Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn Tyr Arg Glu  
 115 120 125  
 Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val Val  
 130 135 140  
 Lys Cys Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile Val Ser Ser  
 145 150 155 160  
 Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg Phe  
 165 170 175  
 Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His Cys  
 180 185 190  
 Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu Ile  
 195 200 205  
 Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln Lys  
 210 215 220  
 Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met Gly  
 225 230 235 240  
 Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly Trp  
 245 250 255  
 Arg Pro Leu Pro Ser Cys Glu Glu Lys Ser Cys Asp Asn Pro Tyr Ile  
 260 265 270  
 Pro Asn Gly Asp Tyr Ser Pro Leu Arg Ile Lys His Arg Thr Gly Asp  
 275 280 285  
 Glu Ile Thr Tyr Gln Cys Arg Asn Gly Phe Tyr Pro Ala Thr Arg Gly  
 290 295 300  
 Asn Thr Ala Lys Cys Thr Ser Thr Gly Trp Ile Pro Ala Pro Arg Cys  
 305 310 315 320  
 Thr Leu Lys Pro Cys Asp Tyr Pro Asp Ile Lys His Gly Gly Leu Tyr  
 325 330 335  
 His Glu Asn Met Arg Arg Pro Tyr Phe Pro Val Ala Val Gly Lys Tyr  
 340 345 350  
 Tyr Ser Tyr Tyr Cys Asp Glu His Phe Glu Thr Pro Ser Gly Ser Tyr

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355          360          365
Trp Asp His Ile His Cys Thr Gln Asp Gly Trp Ser Pro Ala Val Pro
370          375          380

Cys Leu Arg Lys Cys Tyr Phe Pro Tyr Leu Glu Asn Gly Tyr Asn Gln
385          390          395          400

Asn His Gly Arg Lys Phe Val Gln Gly Lys Ser Ile Asp Val Ala Cys
405          410          415

His Pro Gly Tyr Ala Leu Pro Lys Ala Gln Thr Thr Val Thr Cys Met
420          425          430

Glu Asn Gly Trp Ser Pro Thr Pro Arg Cys Ile Arg Val Lys Thr Cys
435          440          445

Ser Lys Ser Ser Ile Asp Ile Glu Asn Gly Phe Ile Ser Glu Ser Gln
450          455          460

Tyr Thr Tyr Ala Leu Lys Glu Lys Ala Lys Tyr Gln Cys Lys Leu Gly
465          470          475          480

Tyr Val Thr Ala Asp Gly Glu Thr Ser Gly Ser Ile Arg Cys Gly Lys
485          490          495

Asp Gly Trp Ser Ala Gln Pro Thr Cys Ile Lys Ser Cys Asp Ile Pro
500          505          510

Val Phe Met Asn Ala Arg Thr Lys Asn Asp Phe Thr Trp Phe Lys Leu
515          520          525

Asn Asp Thr Leu Asp Tyr Glu Cys His Asp Gly Tyr Glu Ser Asn Thr
530          535          540

Gly Ser Thr Thr Gly Ser Ile Val Cys Gly Tyr Asn Gly Trp Ser Asp
545          550          555          560

Leu Pro Ile Cys Tyr Glu Arg Glu Cys Glu Leu Pro Lys Ile Asp Val
565          570          575

His Leu Val Pro Asp Arg Lys Lys Asp Gln Tyr Lys Val Gly Glu Val
580          585          590

Leu Lys Phe Ser Cys Lys Pro Gly Phe Thr Ile Val Gly Pro Asn Ser
595          600          605

Val Gln Cys Tyr His Phe Gly Leu Ser Pro Asp Leu Pro Ile Cys Lys
610          615          620

Glu Gln Val Gln Ser Cys Gly Pro Pro Pro Glu Leu Leu Asn Gly Asn
625          630          635          640

Val Lys Glu Lys Thr Lys Glu Glu Tyr Gly His Ser Glu Val Val Glu
645          650          655

Tyr Tyr Cys Asn Pro Arg Phe Leu Met Lys Gly Pro Asn Lys Ile Gln
660          665          670

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Cys Val Asp Gly Glu Trp Thr Thr Leu Pro Val Cys Ile Val Glu Glu  
 675 680 685  
 Ser Thr Cys Gly Asp Ile Pro Glu Leu Glu His Gly Trp Ala Gln Leu  
 690 695 700  
 Ser Ser Pro Pro Tyr Tyr Tyr Gly Asp Ser Val Glu Phe Asn Cys Ser  
 705 710 715 720  
 Glu Ser Phe Thr Met Ile Gly His Arg Ser Ile Thr Cys Ile His Gly  
 725 730 735  
 Val Trp Thr Gln Leu Pro Gln Cys Val Ala Ile Asp Lys Leu Lys Lys  
 740 745 750  
 Cys Lys Ser Ser Asn Leu Ile Ile Leu Glu Glu His Leu Lys Asn Lys  
 755 760 765  
 Lys Glu Phe Asp His Asn Ser Asn Ile Arg Tyr Arg Cys Arg Gly Lys  
 770 775 780  
 Glu Gly Trp Ile His Thr Val Cys Ile Asn Gly Arg Trp Asp Pro Glu  
 785 790 795 800  
 Val Asn Cys Ser Met Ala Gln Ile Gln Leu Cys Pro Pro Pro Pro Gln  
 805 810 815  
 Ile Pro Asn Ser His Asn Met Thr Thr Thr Leu Asn Tyr Arg Asp Gly  
 820 825 830  
 Glu Lys Val Ser Val Leu Cys Gln Glu Asn Tyr Leu Ile Gln Glu Gly  
 835 840 845  
 Glu Glu Ile Thr Cys Lys Asp Gly Arg Trp Gln Ser Ile Pro Leu Cys  
 850 855 860  
 Val Glu Lys Ile Pro Cys Ser Gln Pro Pro Gln Ile Glu His Gly Thr  
 865 870 875 880  
 Ile Asn Ser Ser Arg Ser Ser Gln Glu Ser Tyr Ala His Gly Thr Lys  
 885 890 895  
 Leu Ser Tyr Thr Cys Glu Gly Gly Phe Arg Ile Ser Glu Glu Asn Glu  
 900 905 910  
 Thr Thr Cys Tyr Met Gly Lys Trp Ser Ser Pro Pro Gln Cys Glu Gly  
 915 920 925  
 Leu Pro Cys Lys Ser Pro Pro Glu Ile Ser His Gly Val Val Ala His  
 930 935 940  
 Met Ser Asp Ser Tyr Gln Tyr Gly Glu Glu Val Thr Tyr Lys Cys Phe  
 945 950 955 960  
 Glu Gly Phe Gly Ile Asp Gly Pro Ala Ile Ala Lys Cys Leu Gly Glu  
 965 970 975  
 Lys Trp Ser His Pro Pro Ser Cys Ile Lys Thr Asp Cys Leu Ser Leu  
 980 985 990

Pro Ser Phe Glu Asn Ala Ile Pro Met Gly Glu Lys Lys Asp Val Tyr  
 995 1000 1005

Lys Ala Gly Glu Gln Val Thr Tyr Thr Cys Ala Thr Tyr Tyr Lys  
 1010 1015 1020

Met Asp Gly Ala Ser Asn Val Thr Cys Ile Asn Ser Arg Trp Thr  
 1025 1030 1035

Gly Arg Pro Thr Cys Arg Asp Thr Ser Cys Val Asn Pro Pro Thr  
 1040 1045 1050

Val Gln Asn Ala Tyr Ile Val Ser Arg Gln Met Ser Lys Tyr Pro  
 1055 1060 1065

Ser Gly Glu Arg Val Arg Tyr Gln Cys Arg Ser Pro Tyr Glu Met  
 1070 1075 1080

Phe Gly Asp Glu Glu Val Met Cys Leu Asn Gly Asn Trp Thr Glu  
 1085 1090 1095

Pro Pro Gln Cys Lys Asp Ser Thr Gly Lys Cys Gly Pro Pro Pro  
 1100 1105 1110

Pro Ile Asp Asn Gly Asp Ile Thr Ser Phe Pro Leu Ser Val Tyr  
 1115 1120 1125

Ala Pro Ala Ser Ser Val Glu Tyr Gln Cys Gln Asn Leu Tyr Gln  
 1130 1135 1140

Leu Glu Gly Asn Lys Arg Ile Thr Cys Arg Asn Gly Gln Trp Ser  
 1145 1150 1155

Glu Pro Pro Lys Cys Leu His Pro Cys Val Ile Ser Arg Glu Ile  
 1160 1165 1170

Met Glu Asn Tyr Asn Ile Ala Leu Arg Trp Thr Ala Lys Gln Lys  
 1175 1180 1185

Leu Tyr Ser Arg Thr Gly Glu Ser Val Glu Phe Val Cys Lys Arg  
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Gly Tyr Arg Leu Ser Ser Arg Ser His Thr Leu Arg Thr Thr Cys  
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Trp Asp Gly Lys Leu Glu Tyr Pro Thr Cys Ala Lys Arg  
 1220 1225 1230

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<400> 147

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 Ala Cys Gln Pro Glu Ser Thr Asp Met Thr Lys Tyr Leu Lys Val Lys  
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 Ala Met Gly Asn Pro Tyr Met Cys Asn Asn Glu Cys Asp Ala Ser Thr  
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 Pro Glu Leu Ala His Pro Pro Glu Leu Met Phe Asp Phe Glu Gly Arg  
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 His Pro Ser Thr Phe Trp Gln Ser Ala Thr Trp Lys Glu Tyr Pro Lys  
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 Thr Asp Asn Ile Val Ile Thr Phe Glu Ser Gly Arg Pro Asp Gln Met  
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 Ile Leu Glu Lys Ser Leu Asp Tyr Gly Arg Thr Trp Gln Pro Tyr Gln  
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 Tyr Tyr Ala Thr Asp Cys Leu Asp Ala Phe His Met Asp Pro Lys Ser  
 180 185 190  
 Val Lys Asp Leu Ser Gln His Thr Val Leu Glu Ile Ile Cys Thr Glu  
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 Glu Tyr Ser Thr Gly Tyr Thr Thr Asn Ser Lys Ile Ile His Phe Glu  
 210 215 220  
 Ile Lys Asp Arg Phe Ala Phe Phe Ala Gly Pro Arg Leu Arg Asn Met  
 225 230 235 240  
 Ala Ser Leu Tyr Gly Gln Leu Asp Thr Thr Lys Lys Leu Arg Asp Phe  
 245 250 255  
 Phe Thr Val Thr Asp Leu Arg Ile Arg Leu Leu Arg Pro Ala Val Gly  
 260 265 270  
 Glu Ile Phe Val Asp Glu Leu His Leu Ala Arg Tyr Phe Tyr Ala Ile  
 275 280 285  
 Ser Asp Ile Lys Val Arg Gly Arg Cys Lys Cys Asn Leu His Ala Thr  
 290 295 300  
 Val Cys Val Tyr Asp Asn Ser Lys Leu Thr Cys Glu Cys Glu His Asn  
 305 310 315 320  
 Thr Thr Gly Pro Asp Cys Gly Lys Cys Lys Lys Asn Tyr Gln Gly Arg  
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 Pro Trp Ser Pro Gly Ser Tyr Leu Pro Ile Pro Lys Gly Thr Ala Asn  
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Thr Cys Ile Pro Ser Ile Ser Ser Ile Gly Ser Lys  
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<400> 148

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Glu Lys Gln Gln Arg Gln Phe Gln Leu Asp Ser Leu Glu Ala Ala Pro  
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Gln Lys Gln Thr Gln Lys Val Glu Asn Glu Lys Thr Glu Gly Thr Asn  
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Leu Lys Arg Glu Asn Gln Arg Leu Met Glu Ile Cys Glu Ser Leu Glu  
 65 70 75 80

Lys Thr Lys Gln Lys Ile Ser His Glu Leu Gln Val Lys Glu Ser Gln  
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Val Asn Phe Gln Glu Gly Gln Leu Asn Ser Gly Lys Lys Gln Ile Glu  
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Lys Leu Glu Gln Glu Leu Lys Arg Cys Lys Ser Glu Leu Glu Arg Ser  
 115 120 125

Gln Gln Ala Ala Gln Ser Ala Asp Val Ser Leu Asn Pro Cys Asn Thr  
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Pro Gln Lys Ile Phe Thr Thr Pro Leu Thr Pro Ser Gln Tyr Tyr Ser  
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Gly Ser Lys Tyr Glu Asp Leu Lys Glu Lys Tyr Asn Lys Glu Val Glu  
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Glu Arg Lys Arg Leu Glu Ala Glu Val Lys Ala Leu Gln Ala Lys Lys  
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Ala Ser Gln Thr Leu Pro Gln Ala Thr Met Asn His Arg Asp Ile Ala  
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Arg His Gln Ala Ser Ser Ser Val Phe Ser Trp Gln Gln Glu Lys Thr  
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Pro Ser His Leu Ser Ser Asn Ser Gln Arg Thr Pro Ile Arg Arg Asp  
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Phe Ser Ala Ser Tyr Phe Ser Gly Glu Leu Glu Val Thr Pro Ser Arg  
 245 250 255

Ser Thr Leu Gln Ile Gly Lys Arg Asp Ala Asn Ser Ser Phe Phe Gly  
 260 265 270

Asn Ser Ser Ser Pro His Leu Leu Asp Gln Leu Lys Ala Gln Asn Gln  
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 Glu Leu Arg Asn Lys Ile Asn Glu Leu Glu Leu Arg Leu Gln Gly His  
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 Glu Lys Glu Met Lys Gly Gln Val Asn Lys Phe Gln Glu Leu Gln Leu  
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 Gln Leu Glu Lys Ala Lys Val Glu Leu Ile Glu Lys Glu Lys Val Leu  
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 340 345 350  
 Ala Ser Thr Lys Tyr Thr Ala Leu Glu Gln Lys Leu Lys Lys Leu Thr  
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 Glu Asp Leu Ser Cys Gln Arg Gln Asn Ala Glu Ser Ala Arg Cys Ser  
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Gln	Ser	Lys	Ile	Asn	His	Leu	Glu	Thr	Cys	Leu	Lys	Thr	Gln	Gln	Ile
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Lys	Ser	His	Glu	Tyr	Asn	Glu	Arg	Val	Arg	Thr	Leu	Glu	Met	Asp	Arg
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Glu	Asn	Leu	Ser	Val	Glu	Ile	Arg	Asn	Leu	His	Asn	Val	Leu	Asp	Ser
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Lys	Ser	Val	Glu	Val	Glu	Thr	Gln	Lys	Leu	Ala	Tyr	Met	Glu	Leu	Gln
		690				695					700				
Gln	Lys	Ala	Glu	Phe	Ser	Asp	Gln	Lys	His	Gln	Lys	Glu	Ile	Glu	Asn
	705					710					715				720
Met	Cys	Leu	Lys	Thr	Ser	Gln	Leu	Thr	Gly	Gln	Val	Glu	Asp	Leu	Glu
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His	Lys	Leu	Gln	Leu	Leu	Ser	Asn	Glu	Ile	Met	Asp	Lys	Asp	Arg	Cys
			740					745					750		
Tyr	Gln	Asp	Leu	His	Ala	Glu	Tyr	Glu	Ser	Leu	Arg	Asp	Leu	Leu	Lys
		755					760					765			
Ser	Lys	Asp	Ala	Ser	Leu	Val	Thr	Asn	Glu	Asp	His	Gln	Arg	Ser	Leu
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Leu	Ala	Phe	Asp	Gln	Gln	Pro	Ala	Met	His	His	Ser	Phe	Ala	Asn	Ile
	785					790					795				800
Ile	Gly	Glu	Gln	Gly	Ser	Met	Pro	Ser	Glu	Arg	Ser	Glu	Cys	Arg	Leu
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Glu	Ala	Asp	Gln	Ser	Pro	Lys	Asn	Ser	Ala	Ile	Leu	Gln	Asn	Arg	Val
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Asp	Ser	Leu	Glu	Phe	Ser	Leu	Glu	Ser	Gln	Lys	Gln	Met	Asn	Ser	Asp
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Leu	Gln	Lys	Gln	Cys	Glu	Glu	Leu	Val	Gln	Ile	Lys	Gly	Glu	Ile	Glu
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Glu	Asn	Leu	Met	Lys	Ala	Glu	Gln	Met	His	Gln	Ser	Phe	Val	Ala	Glu
	865					870					875				880
Thr	Ser	Gln	Arg	Ile	Ser	Lys	Leu	Gln	Glu	Asp	Thr	Ser	Ala	His	Gln
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Asn Val Val Ala Glu Thr Leu Ser Ala Leu Glu Asn Lys Glu Lys Glu  
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 Val Gly Lys Leu Leu Asn Glu Val Lys Ile Leu Asn Asp Asp Ser  
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 1355 1360 1365  
 Phe Gly Glu Gln Pro Asn Glu Gln His Pro Val Ser Leu Ala Pro  
 1370 1375 1380  
 Leu Asp Glu Ser Asn Ser Tyr Glu His Leu Thr Leu Ser Asp Lys  
 1385 1390 1395  
 Glu Val Gln Met His Phe Ala Glu Leu Gln Glu Lys Phe Leu Ser  
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 Leu Gln Ser Glu His Lys Ile Leu His Asp Gln His Cys Gln Met  
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 Ala Glu Asn Leu Val Leu Ser Thr Asn Leu Arg Asn Phe Gln Gly  
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 Asp Leu Val Lys Glu Met Gln Leu Gly Leu Glu Glu Gly Leu Val  
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 Val Tyr Arg Gln Ser Leu Glu Lys Leu Glu Glu Lys Met Glu Ser  
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 Thr Ser Glu Thr Thr Glu Arg Thr Pro Lys His Asp Val His Gln  
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 Ile Cys Asp Lys Asp Ala Gln Gln Asp Leu Asn Leu Asp Ile Glu

1790	1795	1800
Lys Ile Thr Glu Thr Gly Ala Val Lys Pro Thr Gly Glu Cys Ser 1805 1810 1815		
Gly Glu Gln Ser Pro Asp Thr Asn Tyr Glu Pro Pro Gly Glu Asp 1820 1825 1830		
Lys Thr Gln Gly Ser Ser Glu Cys Ile Ser Glu Leu Ser Phe Ser 1835 1840 1845		
Gly Pro Asn Ala Leu Val Pro Met Asp Phe Leu Gly Asn Gln Glu 1850 1855 1860		
Asp Ile His Asn Leu Gln Leu Arg Val Lys Glu Thr Ser Asn Glu 1865 1870 1875		
Asn Leu Arg Leu Leu His Val Ile Glu Asp Arg Asp Arg Lys Val 1880 1885 1890		
Glu Ser Leu Leu Asn Glu Met Lys Glu Leu Asp Ser Lys Leu His 1895 1900 1905		
Leu Gln Glu Val Gln Leu Met Thr Lys Ile Glu Ala Cys Ile Glu 1910 1915 1920		
Leu Glu Lys Ile Val Gly Glu Leu Lys Lys Glu Asn Ser Asp Leu 1925 1930 1935		
Ser Glu Lys Leu Glu Tyr Phe Ser Cys Asp His Gln Glu Leu Leu 1940 1945 1950		
Gln Arg Val Glu Thr Ser Glu Gly Leu Asn Ser Asp Leu Glu Met 1955 1960 1965		
His Ala Asp Lys Ser Ser Arg Glu Asp Ile Gly Asp Asn Val Ala 1970 1975 1980		
Lys Val Asn Asp Ser Trp Lys Glu Arg Phe Leu Asp Val Glu Asn 1985 1990 1995		
Glu Leu Ser Arg Ile Arg Ser Glu Lys Ala Ser Ile Glu His Glu 2000 2005 2010		
Ala Leu Tyr Leu Glu Ala Asp Leu Glu Val Val Gln Thr Glu Lys 2015 2020 2025		
Leu Cys Leu Glu Lys Asp Asn Glu Asn Lys Gln Lys Val Ile Val 2030 2035 2040		
Cys Leu Glu Glu Glu Leu Ser Val Val Thr Ser Glu Arg Asn Gln 2045 2050 2055		
Leu Arg Gly Glu Leu Asp Thr Met Ser Lys Lys Thr Thr Ala Leu 2060 2065 2070		
Asp Gln Leu Ser Glu Lys Met Lys Glu Lys Thr Gln Glu Leu Glu 2075 2080 2085		



Ser His Gln Ser Glu Cys Leu His Cys Ile Gln Val Ala Glu Ala  
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 Lys Glu Met Leu Glu Thr Gln Val Ala His Leu Cys Ser Gln Gln

2975                      2980                      2985  
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          35              40              45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
 50              55              60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65              70              75              80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
      85              90              95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
      100              105

<210> 150
<211> 253
<212> PRT
<213> Homo sapiens

<400> 150

Met Ala Arg Ser Leu Leu Leu Pro Leu Gln Ile Leu Leu Leu Ser Leu
1              5              10              15

Ala Leu Glu Thr Ala Gly Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp
      20              25              30

Gly Ala Pro Cys Ala Arg Gly Ser His Pro Trp Gln Val Ala Leu Leu
      35              40              45

Ser Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn Glu Arg Trp
50              55              60

Val Leu Thr Ala Ala His Cys Lys Met Asn Glu Tyr Thr Val His Leu
65              70              75              80

Gly Ser Asp Thr Leu Gly Asp Arg Arg Ala Gln Arg Ile Lys Ala Ser
      85              90              95

Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp
      100              105              110

Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val
      115              120              125

Lys Lys Val Arg Leu Pro Ser Arg Cys Glu Pro Pro Gly Thr Thr Cys
      130              135              140

Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro
145              150              155              160

Ser Asp Leu Met Cys Val Asp Val Lys Leu Ile Ser Pro Gln Asp Cys
      165              170              175

Thr Lys Val Tyr Lys Asp Leu Leu Glu Asn Ser Met Leu Cys Ala Gly
      180              185              190

Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro
      195              200              205

Leu Val Cys Arg Gly Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Phe

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210                      215                      220  
 Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys  
 225                      230                      235                      240  
  
 Phe Thr Lys Trp Ile Asn Asp Thr Met Lys Lys His Arg  
                     245                      250  
  
 <210> 151  
 <211> 495  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 151  
 Met Val Thr Trp Leu Tyr Arg Phe Leu Pro Thr Ser Asn Met Ala Ala  
 1                      5                      10                      15  
  
 Lys Leu Arg Ser Leu Leu Pro Pro Asp Leu Arg Leu Gln Phe Trp Leu  
                     20                      25                      30  
  
 His Ala Arg Leu Gln Lys Cys Phe Leu Ser Arg Gly Cys Gly Ser Tyr  
                     35                      40                      45  
  
 Cys Ala Gly Ala Lys Ala Ser Pro Leu Pro Gly Lys Met Ala Met Gly  
                     50                      55                      60  
  
 Leu Met Cys Gly Arg Arg Glu Leu Leu Arg Leu Leu Gln Ser Gly Arg  
 65                      70                      75                      80  
  
 Arg Val His Ser Val Ala Gly Pro Ser Gln Trp Leu Gly Lys Pro Leu  
                     85                      90                      95  
  
 Thr Thr Arg Leu Leu Phe Pro Val Ala Pro Cys Cys Cys Arg Pro His  
                     100                      105                      110  
  
 Tyr Leu Phe Leu Ala Ala Ser Gly Pro Arg Ser Leu Ser Thr Ser Ala  
                     115                      120                      125  
  
 Ile Ser Phe Ala Glu Val Gln Val Gln Ala Pro Pro Val Val Ala Ala  
 130                      135                      140  
  
 Thr Pro Ser Pro Thr Ala Val Pro Glu Val Ala Ser Gly Glu Thr Ala  
 145                      150                      155                      160  
  
 Asp Val Val Gln Thr Ala Ala Glu Gln Ser Phe Ala Glu Leu Gly Leu  
                     165                      170                      175  
  
 Gly Ser Tyr Thr Pro Val Gly Leu Ile Gln Asn Leu Leu Glu Phe Met  
                     180                      185                      190  
  
 His Val Asp Leu Gly Leu Pro Trp Trp Gly Ala Ile Ala Ala Cys Thr  
                     195                      200                      205  
  
 Val Phe Ala Arg Cys Leu Ile Phe Pro Leu Ile Val Thr Gly Gln Arg  
 210                      215                      220  
  
 Glu Ala Ala Arg Ile His Asn His Leu Pro Glu Ile Gln Lys Phe Ser  
 225                      230                      235                      240  
  
 Ser Arg Ile Arg Glu Ala Lys Leu Ala Gly Asp His Ile Glu Tyr Tyr

245                      250                      255  
 Lys Ala Ser Ser Glu Met Ala Leu Tyr Gln Lys Lys His Gly Ile Lys  
                          260                      265                      270  
 Leu Tyr Lys Pro Leu Ile Leu Pro Val Thr Gln Ala Pro Ile Phe Ile  
                          275                      280                      285  
 Ser Phe Phe Ile Ala Leu Arg Glu Met Ala Asn Leu Pro Val Pro Ser  
                          290                      295                      300  
 Leu Gln Thr Gly Gly Leu Trp Trp Phe Gln Asp Leu Thr Val Ser Asp  
                          305                      310                      315                      320  
 Pro Ile Tyr Ile Leu Pro Leu Ala Val Thr Ala Thr Met Trp Ala Val  
                          325                      330                      335  
 Leu Glu Leu Gly Ala Glu Thr Gly Val Gln Ser Ser Asp Leu Gln Trp  
                          340                      345                      350  
 Met Arg Asn Val Ile Arg Met Met Pro Leu Ile Thr Leu Pro Ile Thr  
                          355                      360                      365  
 Met His Phe Pro Thr Ala Val Phe Met Tyr Trp Leu Ser Ser Asn Leu  
                          370                      375                      380  
 Phe Ser Leu Val Gln Val Ser Cys Leu Arg Ile Pro Ala Val Arg Thr  
                          385                      390                      395                      400  
 Val Leu Lys Ile Pro Gln Arg Val Val His Asp Leu Asp Lys Leu Pro  
                          405                      410                      415  
 Pro Arg Glu Gly Phe Leu Glu Ser Phe Lys Lys Gly Trp Lys Asn Ala  
                          420                      425                      430  
 Glu Met Thr Arg Gln Leu Arg Glu Arg Glu Gln Arg Met Arg Asn Gln  
                          435                      440                      445  
 Leu Glu Leu Ala Ala Arg Gly Pro Leu Arg Gln Thr Phe Thr His Asn  
                          450                      455                      460  
 Pro Leu Leu Gln Pro Gly Lys Asp Asn Pro Pro Asn Ile Pro Ser Ser  
                          465                      470                      475                      480  
 Ser Ser Lys Pro Lys Ser Lys Tyr Pro Trp His Asp Thr Leu Gly  
                          485                      490                      495

<210> 152  
 <211> 351  
 <212> PRT  
 <213> Homo sapiens

<400> 152

Met Gly Asn Ala Ala Thr Ala Lys Lys Gly Ser Glu Val Glu Ser Val  
1                      5                      10                      15

Lys Glu Phe Leu Ala Lys Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu  
20                      25                      30

Asn Pro Thr Gln Asn Asn Ala Gly Leu Glu Asp Phe Glu Arg Lys Lys

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      35              40              45
Thr Leu Gly Thr Gly Ser Phe Gly Arg Val Met Leu Val Lys His Lys
 50              55              60

Ala Thr Glu Gln Tyr Tyr Ala Met Lys Ile Leu Asp Lys Gln Lys Val
 65              70              75              80

Val Lys Leu Lys Gln Ile Glu His Thr Leu Asn Glu Lys Arg Ile Leu
      85              90              95

Gln Ala Val Asn Phe Pro Phe Leu Val Arg Leu Glu Tyr Ala Phe Lys
      100              105              110

Asp Asn Ser Asn Leu Tyr Met Val Met Glu Tyr Val Pro Gly Gly Glu
      115              120              125

Met Phe Ser His Leu Arg Arg Ile Gly Arg Phe Ser Glu Pro His Ala
      130              135              140

Arg Phe Tyr Ala Ala Gln Ile Val Leu Thr Phe Glu Tyr Leu His Ser
      145              150              155              160

Leu Asp Leu Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu Leu Ile Asp
      165              170              175

His Gln Gly Tyr Ile Gln Val Thr Asp Phe Gly Phe Ala Lys Arg Val
      180              185              190

Lys Gly Arg Thr Trp Thr Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro
      195              200              205

Glu Ile Ile Leu Ser Lys Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala
      210              215              220

Leu Gly Val Leu Ile Tyr Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe
      225              230              235              240

Ala Asp Gln Pro Ile Gln Ile Tyr Glu Lys Ile Val Ser Gly Lys Val
      245              250              255

Arg Phe Pro Ser His Phe Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn
      260              265              270

Leu Leu Gln Val Asp Leu Thr Lys Arg Phe Gly Asn Leu Lys Asn Gly
      275              280              285

Val Ser Asp Ile Lys Thr His Lys Trp Phe Ala Thr Thr Asp Trp Ile
      290              295              300

Ala Ile Tyr Gln Arg Lys Val Glu Ala Pro Phe Ile Pro Lys Phe Arg
      305              310              315              320

Gly Ser Gly Asp Thr Ser Asn Phe Asp Asp Tyr Glu Glu Glu Asp Ile
      325              330              335

Arg Val Ser Ile Thr Glu Lys Cys Ala Lys Glu Phe Gly Glu Phe
      340              345              350

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<210> 153  
 <211> 220  
 <212> PRT  
 <213> Homo sapiens

<400> 153

Met Val Phe Arg Arg Phe Val Glu Val Gly Arg Val Ala Tyr Val Ser  
 1 5 10 15

Phe Gly Pro His Ala Gly Lys Leu Val Ala Ile Val Asp Val Ile Asp  
 20 25 30

Gln Asn Arg Ala Leu Val Asp Gly Pro Cys Thr Gln Val Arg Arg Gln  
 35 40 45

Ala Met Pro Phe Lys Cys Met Gln Leu Thr Asp Phe Ile Leu Lys Phe  
 50 55 60

Leu His Ser Ala His Gln Lys Tyr Val Arg Gln Ala Trp Gln Lys Ala  
 65 70 75 80

Asp Ile Asn Thr Lys Trp Ala Ala Thr Arg Trp Ala Lys Lys Ile Glu  
 85 90 95

Ala Arg Glu Arg Lys Ala Lys Met Thr Asp Phe Asp Arg Phe Lys Val  
 100 105 110

Met Lys Ala Lys Lys Met Arg Asn Arg Ile Ile Lys Asn Glu Val Lys  
 115 120 125

Lys Leu Gln Lys Ala Ala Leu Leu Lys Ala Ser Pro Lys Lys Ala Pro  
 130 135 140

Gly Thr Lys Gly Thr Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala  
 145 150 155 160

Ala Ala Ala Ala Lys Val Pro Ala Lys Lys Ile Thr Ala Ala Ser Lys  
 165 170 175

Lys Ala Pro Ala Gln Lys Val Pro Ala Gln Lys Ala Thr Gly Gln Lys  
 180 185 190

Ala Ala Pro Ala Pro Lys Ala Gln Lys Gly Gln Lys Ala Pro Ala Gln  
 195 200 205

Lys Ala Pro Ala Pro Lys Ala Ser Gly Lys Lys Ala  
 210 215 220

<210> 154  
 <211> 492  
 <212> PRT  
 <213> Homo sapiens

<400> 154

Met Ala Pro Val Gly Val Glu Lys Lys Leu Leu Leu Gly Pro Asn Gly  
 1 5 10 15

Pro Ala Val Ala Ala Ala Gly Asp Leu Thr Ser Glu Glu Glu Glu Gly  
 20 25 30

Gln Ser Leu Trp Ser Ser Ile Leu Ser Glu Val Ser Thr Arg Ala Arg

35	40	45
Ser Lys Leu Pro Ser Gly	Lys Asn Ile Leu Val	Phe Gly Glu Asp Gly
50	55	60
Ser Gly Lys Thr Thr	Leu Met Thr Lys Leu	Gln Gly Ala Glu His Gly
65	70	75 80
Lys Lys Gly Arg Gly	Leu Glu Tyr Leu Tyr	Leu Ser Val His Asp Glu
85	90	95
Asp Arg Asp Asp His Thr	Arg Cys Asn Val Trp Ile	Leu Asp Gly Asp
100	105	110
Leu Tyr His Lys Gly	Leu Leu Lys Phe Ala Val	Ser Ala Glu Ser Leu
115	120	125
Pro Glu Thr Leu Val Ile	Phe Val Ala Asp Met	Ser Arg Pro Trp Thr
130	135	140
Val Met Glu Ser Leu Gln	Lys Trp Ala Ser Val	Leu Arg Glu His Ile
145	150 155	160
Asp Lys Met Lys Ile Pro	Pro Glu Lys Met Arg	Glu Leu Glu Arg Lys
165	170	175
Phe Val Lys Asp Phe Gln	Asp Tyr Met Glu Pro	Glu Glu Gly Cys Gln
180	185	190
Gly Ser Pro Gln Arg Arg	Gly Pro Leu Thr Ser	Gly Ser Asp Glu Glu
195	200	205
Asn Val Ala Leu Pro Leu	Gly Asp Asn Val Leu	Thr His Asn Leu Gly
210	215	220
Ile Pro Val Leu Val Val	Cys Thr Lys Cys Asp	Ala Val Ser Val Leu
225	230 235	240
Glu Lys Glu His Asp Tyr	Arg Asp Glu His Leu	Asp Phe Ile Gln Ser
245	250	255
His Leu Arg Arg Phe Cys	Leu Gln Tyr Gly Ala	Ala Leu Ile Tyr Thr
260	265	270
Ser Val Lys Glu Glu Lys	Asn Leu Asp Leu Leu	Tyr Lys Tyr Ile Val
275	280	285
His Lys Thr Tyr Gly Phe	His Phe Thr Thr Pro	Ala Leu Val Val Glu
290	295	300
Lys Asp Ala Val Phe Ile	Pro Ala Gly Trp Asp	Asn Glu Lys Lys Ile
305	310 315	320
Ala Ile Leu His Glu Asn	Phe Thr Thr Val Lys	Pro Glu Asp Ala Tyr
325	330	335
Glu Asp Phe Ile Val Lys	Pro Pro Val Arg Lys	Leu Val His Asp Lys
340	345	350

Glu Leu Ala Ala Glu Asp Glu Gln Val Phe Leu Met Lys Gln Gln Ser  
355 360 365

Leu Leu Ala Lys Gln Pro Ala Thr Pro Thr Arg Ala Ser Glu Ser Pro  
370 375 380

Ala Arg Gly Pro Ser Gly Ser Pro Arg Thr Gln Gly Arg Gly Gly Pro  
385 390 395 400

Ala Ser Val Pro Ser Ser Ser Pro Gly Thr Ser Val Lys Lys Pro Asp  
405 410 415

Pro Asn Ile Lys Asn Asn Ala Ala Ser Glu Gly Val Leu Ala Ser Phe  
420 425 430

Phe Asn Ser Leu Leu Ser Lys Lys Thr Gly Ser Pro Gly Ser Pro Gly  
435 440 445

Ala Gly Gly Val Gln Ser Thr Ala Lys Lys Ser Gly Gln Lys Thr Val  
450 455 460

Leu Ser Asn Val Gln Glu Glu Leu Asp Arg Met Thr Arg Lys Pro Asp  
465 470 475 480

Ser Met Val Thr Asn Ser Ser Thr Glu Asn Glu Ala  
485 490

<210> 155  
<211> 2230  
<212> PRT  
<213> Homo sapiens

<400> 155

Met Phe Lys Lys Leu Lys Gln Lys Ile Ser Glu Glu Gln Gln Gln Leu  
1 5 10 15

Gln Gln Ala Leu Ala Pro Ala Gln Ala Ser Ser Asn Ser Ser Thr Pro  
20 25 30

Thr Arg Met Arg Ser Arg Thr Ser Ser Phe Thr Glu Gln Leu Asp Glu  
35 40 45

Gly Thr Pro Asn Arg Glu Ser Gly Asp Thr Gln Ser Phe Ala Gln Lys  
50 55 60

Leu Gln Leu Arg Val Pro Ser Val Glu Ser Leu Phe Arg Ser Pro Ile  
65 70 75 80

Lys Glu Ser Leu Phe Arg Ser Ser Ser Lys Glu Ser Leu Val Arg Thr  
85 90 95

Ser Ser Arg Glu Ser Leu Asn Arg Leu Asp Leu Asp Ser Ser Thr Ala  
100 105 110

Ser Phe Asp Pro Pro Ser Asp Met Asp Ser Glu Ala Glu Asp Leu Val  
115 120 125

Gly Asn Ser Asp Ser Leu Asn Lys Glu Gln Leu Ile Gln Arg Leu Arg  
130 135 140

Arg Met Glu Arg Ser Leu Ser Ser Tyr Arg Gly Lys Tyr Ser Glu Leu  
 145 150 155 160  
 Val Thr Ala Tyr Gln Met Leu Gln Arg Glu Lys Lys Lys Leu Gln Gly  
 165 170 175  
 Ile Leu Ser Gln Ser Gln Asp Lys Ser Leu Arg Arg Ile Ala Glu Leu  
 180 185 190  
 Arg Glu Glu Leu Gln Met Asp Gln Gln Ala Lys Lys His Leu Gln Glu  
 195 200 205  
 Glu Phe Asp Ala Ser Leu Glu Glu Lys Asp Gln Tyr Ile Ser Val Leu  
 210 215 220  
 Gln Thr Gln Val Ser Leu Leu Lys Gln Arg Leu Arg Asn Gly Pro Met  
 225 230 235 240  
 Asn Val Asp Val Leu Lys Pro Leu Pro Gln Leu Glu Pro Gln Ala Glu  
 245 250 255  
 Val Phe Thr Lys Glu Glu Asn Pro Glu Ser Asp Gly Glu Pro Val Val  
 260 265 270  
 Glu Asp Gly Thr Ser Val Lys Thr Leu Glu Thr Leu Gln Gln Arg Val  
 275 280 285  
 Lys Arg Gln Glu Asn Leu Leu Lys Arg Cys Lys Glu Thr Ile Gln Ser  
 290 295 300  
 His Lys Glu Gln Cys Thr Leu Leu Thr Ser Glu Lys Glu Ala Leu Gln  
 305 310 315 320  
 Glu Gln Leu Asp Glu Arg Leu Gln Glu Leu Glu Lys Ile Lys Asp Leu  
 325 330 335  
 His Met Ala Glu Lys Thr Lys Leu Ile Thr Gln Leu Arg Asp Ala Lys  
 340 345 350  
 Asn Leu Ile Glu Gln Leu Glu Gln Asp Lys Gly Met Val Ile Ala Glu  
 355 360 365  
 Thr Lys Arg Gln Met His Glu Thr Leu Glu Met Lys Glu Glu Glu Ile  
 370 375 380  
 Ala Gln Leu Arg Ser Arg Ile Lys Gln Met Thr Thr Gln Gly Glu Glu  
 385 390 395 400  
 Leu Arg Glu Gln Lys Glu Lys Ser Glu Arg Ala Ala Phe Glu Glu Leu  
 405 410 415  
 Glu Lys Ala Leu Ser Thr Ala Gln Lys Thr Glu Glu Ala Arg Arg Lys  
 420 425 430  
 Leu Lys Ala Glu Met Asp Glu Gln Ile Lys Thr Ile Glu Lys Thr Ser  
 435 440 445  
 Glu Glu Glu Arg Ile Ser Leu Gln Gln Glu Leu Ser Arg Val Lys Gln  
 450 455 460

Glu Val Val Asp Val Met Lys Lys Ser Ser Glu Glu Gln Ile Ala Lys  
 465 470 475 480  
 Leu Gln Lys Leu His Glu Lys Glu Leu Ala Arg Lys Glu Gln Glu Leu  
 485 490 495  
 Thr Lys Lys Leu Gln Thr Arg Glu Arg Glu Phe Gln Glu Gln Met Lys  
 500 505 510  
 Val Ala Leu Glu Lys Ser Gln Ser Glu Tyr Leu Lys Ile Ser Gln Glu  
 515 520 525  
 Lys Glu Gln Gln Glu Ser Leu Ala Leu Glu Glu Leu Glu Leu Gln Lys  
 530 535 540  
 Lys Ala Ile Leu Thr Glu Ser Glu Asn Lys Leu Arg Asp Leu Gln Gln  
 545 550 555 560  
 Glu Ala Glu Thr Tyr Arg Thr Arg Ile Leu Glu Leu Glu Ser Ser Leu  
 565 570 575  
 Glu Lys Ser Leu Gln Glu Asn Lys Asn Gln Ser Lys Asp Leu Ala Val  
 580 585 590  
 His Leu Glu Ala Glu Lys Asn Lys His Asn Lys Glu Ile Thr Val Met  
 595 600 605  
 Val Glu Lys His Lys Thr Glu Leu Glu Ser Leu Lys His Gln Gln Asp  
 610 615 620  
 Ala Leu Trp Thr Glu Lys Leu Gln Val Leu Lys Gln Gln Tyr Gln Thr  
 625 630 635 640  
 Glu Met Glu Lys Leu Arg Glu Lys Cys Glu Gln Glu Lys Glu Thr Leu  
 645 650 655  
 Leu Lys Asp Lys Glu Ile Ile Phe Gln Ala His Ile Glu Glu Met Asn  
 660 665 670  
 Glu Lys Thr Leu Glu Lys Leu Asp Val Lys Gln Thr Glu Leu Glu Ser  
 675 680 685  
 Leu Ser Ser Glu Leu Ser Glu Val Leu Lys Ala Arg His Lys Leu Glu  
 690 695 700  
 Glu Glu Leu Ser Val Leu Lys Asp Gln Thr Asp Lys Met Lys Gln Glu  
 705 710 715 720  
 Leu Glu Ala Lys Met Asp Glu Gln Lys Asn His His Gln Gln Gln Val  
 725 730 735  
 Asp Ser Ile Ile Lys Glu His Glu Val Ser Ile Gln Arg Thr Glu Lys  
 740 745 750  
 Ala Leu Lys Asp Gln Ile Asn Gln Leu Glu Leu Leu Leu Lys Glu Arg  
 755 760 765  
 Asp Lys His Leu Lys Glu His Gln Ala His Val Glu Asn Leu Glu Ala  
 770 775 780

Asp Ile Lys Arg Ser Glu Gly Glu Leu Gln Gln Ala Ser Ala Lys Leu  
 785 790 795 800  
 Asp Val Phe Gln Ser Tyr Gln Ser Ala Thr His Glu Gln Thr Lys Ala  
 805 810 815  
 Tyr Glu Glu Gln Leu Ala Gln Leu Gln Gln Lys Leu Leu Asp Leu Glu  
 820 825 830  
 Thr Glu Arg Ile Leu Leu Thr Lys Gln Val Ala Glu Val Glu Ala Gln  
 835 840 845  
 Lys Lys Asp Val Cys Thr Glu Leu Asp Ala His Lys Ile Gln Val Gln  
 850 855 860  
 Asp Leu Met Gln Gln Leu Glu Lys Gln Asn Ser Glu Met Glu Gln Lys  
 865 870 875 880  
 Val Lys Ser Leu Thr Gln Val Tyr Glu Ser Lys Leu Glu Asp Gly Asn  
 885 890 895  
 Lys Glu Gln Glu Gln Thr Lys Gln Ile Leu Val Glu Lys Glu Asn Met  
 900 905 910  
 Ile Leu Gln Met Arg Glu Gly Gln Lys Lys Glu Ile Glu Ile Leu Thr  
 915 920 925  
 Gln Lys Leu Ser Ala Lys Glu Asp Ser Ile His Ile Leu Asn Glu Glu  
 930 935 940  
 Tyr Glu Thr Lys Phe Lys Asn Gln Glu Lys Lys Met Glu Lys Val Lys  
 945 950 955 960  
 Gln Lys Ala Lys Glu Met Gln Glu Thr Leu Lys Lys Lys Leu Leu Asp  
 965 970 975  
 Gln Glu Ala Lys Leu Lys Lys Glu Leu Glu Asn Thr Ala Leu Glu Leu  
 980 985 990  
 Ser Gln Lys Glu Lys Gln Phe Asn Ala Lys Met Leu Glu Met Ala Gln  
 995 1000 1005  
 Ala Asn Ser Ala Gly Ile Ser Asp Ala Val Ser Arg Leu Glu Thr  
 1010 1015 1020  
 Asn Gln Lys Glu Gln Ile Glu Ser Leu Thr Glu Val His Arg Arg  
 1025 1030 1035  
 Glu Leu Asn Asp Val Ile Ser Ile Trp Glu Lys Lys Leu Asn Gln  
 1040 1045 1050  
 Gln Ala Glu Glu Leu Gln Glu Ile His Glu Ile Gln Leu Gln Glu  
 1055 1060 1065  
 Lys Glu Gln Glu Val Ala Glu Leu Lys Gln Lys Ile Leu Leu Phe  
 1070 1075 1080  
 Gly Cys Glu Lys Glu Glu Met Asn Lys Glu Ile Thr Trp Leu Lys

1085	1090	1095
Glu Glu Gly Val Lys Gln Asp Thr Thr Leu Asn Glu Leu Gln Glu 1100 1105 1110		
Gln Leu Lys Gln Lys Ser Ala His Val Asn Ser Leu Ala Gln Asp 1115 1120 1125		
Glu Thr Lys Leu Lys Ala His Leu Glu Lys Leu Glu Val Asp Leu 1130 1135 1140		
Asn Lys Ser Leu Lys Glu Asn Thr Phe Leu Gln Glu Gln Leu Val 1145 1150 1155		
Glu Leu Lys Met Leu Ala Glu Glu Asp Lys Arg Lys Val Ser Glu 1160 1165 1170		
Leu Thr Ser Lys Leu Lys Thr Thr Asp Glu Glu Phe Gln Ser Leu 1175 1180 1185		
Lys Ser Ser His Glu Lys Ser Asn Lys Ser Leu Glu Asp Lys Ser 1190 1195 1200		
Leu Glu Phe Lys Lys Leu Ser Glu Glu Leu Ala Ile Gln Leu Asp 1205 1210 1215		
Ile Cys Cys Lys Lys Thr Glu Ala Leu Leu Glu Ala Lys Thr Asn 1220 1225 1230		
Glu Leu Ile Asn Ile Ser Ser Ser Lys Thr Asn Ala Ile Leu Ser 1235 1240 1245		
Arg Ile Ser His Cys Gln His Arg Thr Thr Lys Val Lys Glu Ala 1250 1255 1260		
Leu Leu Ile Lys Thr Cys Thr Val Ser Glu Leu Glu Ala Gln Leu 1265 1270 1275		
Arg Gln Leu Thr Glu Glu Gln Asn Thr Leu Asn Ile Ser Phe Gln 1280 1285 1290		
Gln Ala Thr His Gln Leu Glu Glu Lys Glu Asn Gln Ile Lys Ser 1295 1300 1305		
Met Lys Ala Asp Ile Glu Ser Leu Val Thr Glu Lys Glu Ala Leu 1310 1315 1320		
Gln Lys Glu Gly Gly Asn Gln Gln Gln Ala Ala Ser Glu Lys Glu 1325 1330 1335		
Ser Cys Ile Thr Gln Leu Lys Lys Glu Leu Ser Glu Asn Ile Asn 1340 1345 1350		
Ala Val Thr Leu Met Lys Glu Glu Leu Lys Glu Lys Lys Val Glu 1355 1360 1365		
Ile Ser Ser Leu Ser Lys Gln Leu Thr Asp Leu Asn Val Gln Leu 1370 1375 1380		

Gln Asn Ser Ile Ser Leu Ser Glu Lys Glu Ala Ala Ile Ser Ser  
 1385 1390 1395  
 Leu Arg Lys Gln Tyr Asp Glu Glu Lys Cys Glu Leu Leu Asp Gln  
 1400 1405 1410  
 Val Gln Asp Leu Ser Phe Lys Val Asp Thr Leu Ser Lys Glu Lys  
 1415 1420 1425  
 Ile Ser Ala Leu Glu Gln Val Asp Asp Trp Ser Asn Lys Phe Ser  
 1430 1435 1440  
 Glu Trp Lys Lys Lys Ala Gln Ser Arg Phe Thr Gln His Gln Asn  
 1445 1450 1455  
 Thr Val Lys Glu Leu Gln Ile Gln Leu Glu Leu Lys Ser Lys Glu  
 1460 1465 1470  
 Ala Tyr Glu Lys Asp Glu Gln Ile Asn Leu Leu Lys Glu Glu Leu  
 1475 1480 1485  
 Asp Gln Gln Asn Lys Arg Phe Asp Cys Leu Lys Gly Glu Met Glu  
 1490 1495 1500  
 Asp Asp Lys Ser Lys Met Glu Lys Lys Glu Ser Asn Leu Glu Thr  
 1505 1510 1515  
 Glu Leu Lys Ser Gln Thr Ala Arg Ile Met Glu Leu Glu Asp His  
 1520 1525 1530  
 Ile Thr Gln Lys Thr Ile Glu Ile Glu Ser Leu Asn Glu Val Leu  
 1535 1540 1545  
 Lys Asn Tyr Asn Gln Gln Lys Asp Ile Glu His Lys Glu Leu Val  
 1550 1555 1560  
 Gln Lys Leu Gln His Phe Gln Glu Leu Gly Glu Glu Lys Asp Asn  
 1565 1570 1575  
 Arg Val Lys Glu Ala Glu Glu Lys Ile Leu Thr Leu Glu Asn Gln  
 1580 1585 1590  
 Val Tyr Ser Met Lys Ala Glu Leu Glu Thr Lys Lys Lys Glu Leu  
 1595 1600 1605  
 Glu His Val Asn Leu Ser Val Lys Ser Lys Glu Glu Glu Leu Lys  
 1610 1615 1620  
 Ala Leu Glu Asp Arg Leu Glu Ser Glu Ser Ala Ala Lys Leu Ala  
 1625 1630 1635  
 Glu Leu Lys Arg Lys Ala Glu Gln Lys Ile Ala Ala Ile Lys Lys  
 1640 1645 1650  
 Gln Leu Leu Ser Gln Met Glu Glu Lys Glu Glu Gln Tyr Lys Lys  
 1655 1660 1665  
 Gly Thr Glu Ser His Leu Ser Glu Leu Asn Thr Lys Leu Gln Glu  
 1670 1675 1680



Arg Glu Arg Glu Val His Ile Leu Glu Glu Lys Leu Lys Ser Val  
 1685 1690 1695  
 Glu Ser Ser Gln Ser Glu Thr Leu Ile Val Pro Arg Ser Ala Lys  
 1700 1705 1710  
 Asn Val Ala Ala Tyr Thr Glu Gln Glu Glu Ala Asp Ser Gln Gly  
 1715 1720 1725  
 Cys Val Gln Lys Thr Tyr Glu Glu Lys Ile Ser Val Leu Gln Arg  
 1730 1735 1740  
 Asn Leu Thr Glu Lys Glu Lys Leu Leu Gln Arg Val Gly Gln Glu  
 1745 1750 1755  
 Lys Glu Glu Thr Val Ser Ser His Phe Glu Met Arg Cys Gln Tyr  
 1760 1765 1770  
 Gln Glu Arg Leu Ile Lys Leu Glu His Ala Glu Ala Lys Gln His  
 1775 1780 1785  
 Glu Asp Gln Ser Met Ile Gly His Leu Gln Glu Glu Leu Glu Glu  
 1790 1795 1800  
 Lys Asn Lys Lys Tyr Ser Leu Ile Val Ala Gln His Val Glu Lys  
 1805 1810 1815  
 Glu Gly Gly Lys Asn Asn Ile Gln Ala Lys Gln Asn Leu Glu Asn  
 1820 1825 1830  
 Val Phe Asp Asp Val Gln Lys Thr Leu Gln Glu Lys Glu Leu Thr  
 1835 1840 1845  
 Cys Gln Ile Leu Glu Gln Lys Ile Lys Glu Leu Asp Ser Cys Leu  
 1850 1855 1860  
 Val Arg Gln Lys Glu Val His Arg Val Glu Met Glu Glu Leu Thr  
 1865 1870 1875  
 Ser Lys Tyr Glu Lys Leu Gln Ala Leu Gln Gln Met Asp Gly Arg  
 1880 1885 1890  
 Asn Lys Pro Thr Glu Leu Leu Glu Glu Asn Thr Glu Glu Lys Ser  
 1895 1900 1905  
 Lys Ser His Leu Val Gln Pro Lys Leu Leu Ser Asn Met Glu Ala  
 1910 1915 1920  
 Gln His Asn Asp Leu Glu Phe Lys Leu Ala Gly Ala Glu Arg Glu  
 1925 1930 1935  
 Lys Gln Lys Leu Gly Lys Glu Ile Val Arg Leu Gln Lys Asp Leu  
 1940 1945 1950  
 Arg Met Leu Arg Lys Glu His Gln Gln Glu Leu Glu Ile Leu Lys  
 1955 1960 1965  
 Lys Glu Tyr Asp Gln Glu Arg Glu Glu Lys Ile Lys Gln Glu Gln  
 1970 1975 1980

Glu Asp Leu Glu Leu Lys His Asn Ser Thr Leu Lys Gln Leu Met  
 1985 1990 1995  
 Arg Glu Phe Asn Thr Gln Leu Ala Gln Lys Glu Gln Glu Leu Glu  
 2000 2005 2010  
 Met Thr Ile Lys Glu Thr Ile Asn Lys Ala Gln Glu Val Glu Ala  
 2015 2020 2025  
 Glu Leu Leu Glu Ser His Gln Glu Glu Thr Asn Gln Leu Leu Lys  
 2030 2035 2040  
 Lys Ile Ala Glu Lys Asp Asp Asp Leu Lys Arg Thr Ala Lys Arg  
 2045 2050 2055  
 Tyr Glu Glu Ile Leu Asp Ala Arg Glu Glu Glu Met Thr Ala Lys  
 2060 2065 2070  
 Val Arg Asp Leu Gln Thr Gln Leu Glu Glu Leu Gln Lys Lys Tyr  
 2075 2080 2085  
 Gln Gln Lys Leu Glu Gln Glu Glu Asn Pro Gly Asn Asp Asn Val  
 2090 2095 2100  
 Thr Ile Met Glu Leu Gln Thr Gln Leu Ala Gln Lys Thr Thr Leu  
 2105 2110 2115  
 Ile Ser Asp Ser Lys Leu Lys Glu Gln Glu Phe Arg Glu Gln Ile  
 2120 2125 2130  
 His Asn Leu Glu Asp Arg Leu Lys Lys Tyr Glu Lys Asn Val Tyr  
 2135 2140 2145  
 Ala Thr Thr Val Gly Thr Pro Tyr Lys Gly Gly Asn Leu Tyr His  
 2150 2155 2160  
 Thr Asp Val Ser Leu Phe Gly Glu Pro Thr Glu Phe Glu Tyr Leu  
 2165 2170 2175  
 Arg Lys Val Leu Phe Glu Tyr Met Met Gly Arg Glu Thr Lys Thr  
 2180 2185 2190  
 Met Ala Lys Val Ile Thr Thr Val Leu Lys Phe Pro Asp Asp Gln  
 2195 2200 2205  
 Thr Gln Lys Ile Leu Glu Arg Glu Asp Ala Arg Leu Met Phe Thr  
 2210 2215 2220  
 Ser Pro Arg Ser Gly Ile Phe  
 2225 2230

<210> 156  
 <211> 719  
 <212> PRT  
 <213> Homo sapiens

<400> 156

Glu Ile Met Glu Glu Leu Arg Ser Leu Asp Pro Arg Arg Gln Glu Leu  
 1 5 10 15

Leu Glu Ala Arg Phe Thr Gly Val Gly Val Ser Lys Gly Pro Leu Asn  
 20 25 30  
 Ser Glu Ser Ser Asn Gln Ser Leu Cys Ser Val Gly Ser Leu Ser Asp  
 35 40 45  
 Lys Glu Val Glu Thr Pro Glu Lys Lys Gln Asn Asp Gln Arg Asn Arg  
 50 55 60  
 Lys Arg Lys Ala Glu Pro Tyr Glu Thr Ser Gln Gly Lys Gly Thr Pro  
 65 70 75 80  
 Arg Gly His Lys Ile Ser Asp Tyr Phe Glu Arg Arg Val Glu Gln Pro  
 85 90 95  
 Leu Tyr Gly Leu Asp Gly Ser Ala Ala Lys Glu Ala Thr Glu Glu Gln  
 100 105 110  
 Ser Ala Leu Pro Thr Leu Met Ser Val Met Leu Ala Lys Pro Arg Leu  
 115 120 125  
 Asp Pro Glu Gln Leu Ala Gln Arg Gly Ala Gly Leu Cys Phe Thr Phe  
 130 135 140  
 Val Ser Ala Gln Gln Asn Ser Pro Ser Ser Thr Gly Ser Gly Asn Thr  
 145 150 155 160  
 Glu His Ser Cys Ser Ser Gln Lys Gln Ile Ser Ile Gln His Arg Gln  
 165 170 175  
 Thr Gln Ser Asp Leu Thr Ile Glu Lys Ile Ser Ala Leu Glu Asn Ser  
 180 185 190  
 Lys Asn Ser Asp Leu Glu Lys Lys Glu Gly Arg Ile Asp Asp Leu Leu  
 195 200 205  
 Arg Ala Asn Cys Asp Leu Arg Arg Gln Ile Asp Glu Gln Gln Lys Met  
 210 215 220  
 Leu Glu Lys Tyr Lys Glu Arg Leu Asn Arg Cys Val Thr Met Ser Lys  
 225 230 235 240  
 Lys Leu Leu Ile Glu Lys Ser Lys Gln Glu Lys Met Ala Cys Arg Asp  
 245 250 255  
 Lys Ser Met Gln Asp Arg Leu Arg Leu Gly His Phe Thr Thr Val Arg  
 260 265 270  
 His Gly Ala Ser Phe Thr Glu Gln Trp Thr Asp Gly Tyr Ala Phe Gln  
 275 280 285  
 Asn Leu Ile Lys Gln Gln Glu Arg Ile Asn Ser Gln Arg Glu Glu Ile  
 290 295 300  
 Glu Arg Gln Arg Lys Met Leu Ala Lys Arg Lys Pro Pro Ala Met Gly  
 305 310 315 320  
 Gln Ala Pro Pro Ala Thr Asn Glu Gln Lys Gln Arg Lys Ser Lys Thr



Asn Thr Ile Leu Lys Ala Thr Glu Val Gln Phe Pro Pro Lys Pro Val  
645 650 655

Val Thr Pro Glu Ala Lys Ala Phe Ile Arg Arg Cys Leu Ala Tyr Arg  
660 665 670

Lys Glu Asp Arg Ile Asp Val Gln Gln Leu Ala Cys Asp Pro Tyr Leu  
675 680 685

Leu Pro His Ile Arg Lys Ser Val Ser Thr Ser Ser Pro Ala Gly Ala  
690 695 700

Ala Ile Ala Ser Thr Ser Gly Ala Ser Asn Asn Ser Ser Ser Asn  
705 710 715

<210> 157  
<211> 1976  
<212> PRT  
<213> Homo sapiens

<400> 157

Met Ala Gln Arg Thr Gly Leu Glu Asp Pro Glu Arg Tyr Leu Phe Val  
1 5 10 15

Asp Arg Ala Val Ile Tyr Asn Pro Ala Thr Gln Ala Asp Trp Thr Ala  
20 25 30

Lys Lys Leu Val Trp Ile Pro Ser Glu Arg His Gly Phe Glu Ala Ala  
35 40 45

Ser Ile Lys Glu Glu Arg Gly Asp Glu Val Met Val Glu Leu Ala Glu  
50 55 60

Asn Gly Lys Lys Ala Met Val Asn Lys Asp Asp Ile Gln Lys Met Asn  
65 70 75 80

Pro Pro Lys Phe Ser Lys Val Glu Asp Met Ala Glu Leu Thr Cys Leu  
85 90 95

Asn Glu Ala Ser Val Leu His Asn Leu Lys Asp Arg Tyr Tyr Ser Gly  
100 105 110

Leu Ile Tyr Thr Tyr Ser Gly Leu Phe Cys Val Val Ile Asn Pro Tyr  
115 120 125

Lys Asn Leu Pro Ile Tyr Ser Glu Asn Ile Ile Glu Met Tyr Arg Gly  
130 135 140

Lys Lys Arg His Glu Met Pro Pro His Ile Tyr Ala Ile Ser Glu Ser  
145 150 155 160

Ala Tyr Arg Cys Met Leu Gln Asp Arg Glu Asp Gln Ser Ile Leu Cys  
165 170 175

Thr Gly Glu Ser Gly Ala Gly Lys Thr Glu Asn Thr Lys Lys Val Ile  
180 185 190

Gln Tyr Leu Ala His Val Ala Ser Ser His Lys Gly Arg Lys Asp His  
195 200 205

Asn Ile Pro Gly Glu Leu Glu Arg Gln Leu Leu Gln Ala Asn Pro Ile  
 210 215 220  
 Leu Glu Ser Phe Gly Asn Ala Lys Thr Val Lys Asn Asp Asn Ser Ser  
 225 230 235 240  
 Arg Phe Gly Lys Phe Ile Arg Ile Asn Phe Asp Val Thr Gly Tyr Ile  
 245 250 255  
 Val Gly Ala Asn Ile Glu Thr Tyr Leu Leu Glu Lys Ser Arg Ala Val  
 260 265 270  
 Arg Gln Ala Lys Asp Glu Arg Thr Phe His Ile Phe Tyr Gln Leu Leu  
 275 280 285  
 Ser Gly Ala Gly Glu His Leu Lys Ser Asp Leu Leu Leu Glu Gly Phe  
 290 295 300  
 Asn Asn Tyr Arg Phe Leu Ser Asn Gly Tyr Ile Pro Ile Pro Gly Gln  
 305 310 315 320  
 Gln Asp Lys Asp Asn Phe Gln Glu Thr Met Glu Ala Met His Ile Met  
 325 330 335  
 Gly Phe Ser His Glu Glu Ile Leu Ser Met Leu Lys Val Val Ser Ser  
 340 345 350  
 Val Leu Gln Phe Gly Asn Ile Ser Phe Lys Lys Glu Arg Asn Thr Asp  
 355 360 365  
 Gln Ala Ser Met Pro Glu Asn Thr Val Ala Gln Lys Leu Cys His Leu  
 370 375 380  
 Leu Gly Met Asn Val Met Glu Phe Thr Arg Ala Ile Leu Thr Pro Arg  
 385 390 395 400  
 Ile Lys Val Gly Arg Asp Tyr Val Gln Lys Ala Gln Thr Lys Glu Gln  
 405 410 415  
 Ala Asp Phe Ala Val Glu Ala Leu Ala Lys Ala Thr Tyr Glu Arg Leu  
 420 425 430  
 Phe Arg Trp Leu Val His Arg Ile Asn Lys Ala Leu Asp Arg Thr Lys  
 435 440 445  
 Arg Gln Gly Ala Ser Phe Ile Gly Ile Leu Asp Ile Ala Gly Phe Glu  
 450 455 460  
 Ile Phe Glu Leu Asn Ser Phe Glu Gln Leu Cys Ile Asn Tyr Thr Asn  
 465 470 475 480  
 Glu Lys Leu Gln Gln Leu Phe Asn His Thr Met Phe Ile Leu Glu Gln  
 485 490 495  
 Glu Glu Tyr Gln Arg Glu Gly Ile Glu Trp Asn Phe Ile Asp Phe Gly  
 500 505 510  
 Leu Asp Leu Gln Pro Cys Ile Asp Leu Ile Glu Arg Pro Ala Asn Pro  
 515 520 525

Pro Gly Val Leu Ala Leu Leu Asp Glu Glu Cys Trp Phe Pro Lys Ala  
 530 535 540  
 Thr Asp Lys Thr Phe Val Glu Lys Leu Val Gln Glu Gln Gly Ser His  
 545 550 555 560  
 Ser Lys Phe Gln Lys Pro Arg Gln Leu Lys Asp Lys Ala Asp Phe Cys  
 565 570 575  
 Ile Ile His Tyr Ala Gly Lys Val Asp Tyr Lys Ala Asp Glu Trp Leu  
 580 585 590  
 Met Lys Asn Met Asp Pro Leu Asn Asp Asn Val Ala Thr Leu Leu His  
 595 600 605  
 Gln Ser Ser Asp Arg Phe Val Ala Glu Leu Trp Lys Asp Val Asp Arg  
 610 615 620  
 Ile Val Gly Leu Asp Gln Val Thr Gly Met Thr Glu Thr Ala Phe Gly  
 625 630 635 640  
 Ser Ala Tyr Lys Thr Lys Lys Gly Met Phe Arg Thr Val Gly Gln Leu  
 645 650 655  
 Tyr Lys Glu Ser Leu Thr Lys Leu Met Ala Thr Leu Arg Asn Thr Asn  
 660 665 670  
 Pro Asn Phe Val Arg Cys Ile Ile Pro Asn His Glu Lys Arg Ala Gly  
 675 680 685  
 Lys Leu Asp Pro His Leu Val Leu Asp Gln Leu Arg Cys Asn Gly Val  
 690 695 700  
 Leu Glu Gly Ile Arg Ile Cys Arg Gln Gly Phe Pro Asn Arg Ile Val  
 705 710 715 720  
 Phe Gln Glu Phe Arg Gln Arg Tyr Glu Ile Leu Thr Pro Asn Ala Ile  
 725 730 735  
 Pro Lys Gly Phe Met Asp Gly Lys Gln Ala Cys Glu Arg Met Ile Arg  
 740 745 750  
 Ala Leu Glu Leu Asp Pro Asn Leu Tyr Arg Ile Gly Gln Ser Lys Ile  
 755 760 765  
 Phe Phe Arg Ala Gly Val Leu Ala His Leu Glu Glu Glu Arg Asp Leu  
 770 775 780  
 Lys Ile Thr Asp Ile Ile Ile Phe Phe Gln Ala Val Cys Arg Gly Cys  
 785 790 795 800  
 Leu Ala Arg Lys Ala Phe Ala Lys Lys Gln Gln Gln Leu Ser Ala Leu  
 805 810 815  
 Lys Val Leu Gln Arg Asn Cys Ala Ala Tyr Leu Lys Leu Arg His Trp  
 820 825 830  
 Gln Trp Trp Arg Val Phe Thr Lys Val Lys Pro Leu Leu Gln Val Thr  
 835 840 845

Arg Gln Glu Glu Glu Leu Gln Ala Lys Asp Glu Glu Leu Leu Lys Val  
 850 855 860  
 Lys Glu Lys Gln Thr Lys Val Glu Gly Glu Leu Glu Glu Met Glu Arg  
 865 870 875 880  
 Lys His Gln Gln Leu Leu Glu Glu Lys Asn Ile Leu Ala Glu Gln Leu  
 885 890 895  
 Gln Ala Glu Thr Glu Leu Phe Ala Glu Ala Glu Glu Met Arg Ala Arg  
 900 905 910  
 Leu Ala Ala Lys Lys Gln Glu Leu Glu Glu Ile Leu His Asp Leu Glu  
 915 920 925  
 Ser Arg Val Glu Glu Glu Glu Glu Arg Asn Gln Ile Leu Gln Asn Glu  
 930 935 940  
 Lys Lys Lys Met Gln Ala His Ile Gln Asp Leu Glu Glu Gln Leu Asp  
 945 950 955 960  
 Glu Glu Glu Gly Ala Arg Gln Lys Leu Gln Leu Glu Lys Val Thr Ala  
 965 970 975  
 Glu Ala Lys Ile Lys Lys Met Glu Glu Glu Ile Leu Leu Leu Glu Asp  
 980 985 990  
 Gln Asn Ser Lys Phe Ile Lys Glu Lys Lys Leu Met Glu Asp Arg Ile  
 995 1000 1005  
 Ala Glu Cys Ser Ser Gln Leu Ala Glu Glu Glu Glu Lys Ala Lys  
 1010 1015 1020  
 Asn Leu Ala Lys Ile Arg Asn Lys Gln Glu Val Met Ile Ser Asp  
 1025 1030 1035  
 Leu Glu Glu Arg Leu Lys Lys Glu Glu Lys Thr Arg Gln Glu Leu  
 1040 1045 1050  
 Glu Lys Ala Lys Arg Lys Leu Asp Gly Glu Thr Thr Asp Leu Gln  
 1055 1060 1065  
 Asp Gln Ile Ala Glu Leu Gln Ala Gln Ile Asp Glu Leu Lys Leu  
 1070 1075 1080  
 Gln Leu Ala Lys Lys Glu Glu Glu Leu Gln Gly Ala Leu Ala Arg  
 1085 1090 1095  
 Gly Asp Asp Glu Thr Leu His Lys Asn Asn Ala Leu Lys Val Val  
 1100 1105 1110  
 Arg Glu Leu Gln Ala Gln Ile Ala Glu Leu Gln Glu Asp Phe Glu  
 1115 1120 1125  
 Ser Glu Lys Ala Ser Arg Asn Lys Ala Glu Lys Gln Lys Arg Asp  
 1130 1135 1140  
 Leu Ser Glu Glu Leu Glu Ala Leu Lys Thr Glu Leu Glu Asp Thr



1145	1150	1155
Leu Asp Thr Thr Ala Ala Gln 1160 1165	Gln Glu Leu Arg Thr 1170	Lys Arg Glu
Gln Glu Val Ala Glu Leu Lys 1175 1180	Lys Ala Leu Glu Glu 1185	Glu Thr Lys
Asn His Glu Ala Gln Ile Gln 1190 1195	Asp Met Arg Gln Arg 1200	His Ala Thr
Ala Leu Glu Glu Leu Ser Glu 1205 1210	Gln Leu Glu Gln Ala 1215	Lys Arg Phe
Lys Ala Asn Leu Glu Lys Asn 1220 1225	Lys Gln Gly Leu Glu 1230	Thr Asp Asn
Lys Glu Leu Ala Cys Glu Val 1235 1240	Lys Val Leu Gln Gln 1245	Val Lys Ala
Glu Ser Glu His Lys Arg Lys 1250 1255	Lys Leu Asp Ala Gln 1260	Val Gln Glu
Leu His Ala Lys Val Ser Glu 1265 1270	Gly Asp Arg Leu Arg 1275	Val Glu Leu
Ala Glu Lys Ala Ser Lys Leu 1280 1285	Gln Asn Glu Leu Asp 1290	Asn Val Ser
Thr Leu Leu Glu Glu Ala Glu 1295 1300	Lys Lys Gly Ile Lys 1305	Phe Ala Lys
Asp Ala Ala Ser Leu Glu Ser 1310 1315	Gln Leu Gln Asp Thr 1320	Gln Glu Leu
Leu Gln Glu Glu Thr Arg Gln 1325 1330	Lys Leu Asn Leu Ser 1335	Ser Arg Ile
Arg Gln Leu Glu Glu Glu Lys 1340 1345	Asn Ser Leu Gln Glu 1350	Gln Gln Glu
Glu Glu Glu Glu Ala Arg Lys 1355 1360	Asn Leu Glu Lys Gln 1365	Val Leu Ala
Leu Gln Ser Gln Leu Ala Asp 1370 1375	Thr Lys Lys Lys Val 1380	Asp Asp Asp
Leu Gly Thr Ile Glu Ser Leu 1385 1390	Glu Glu Ala Lys Lys 1395	Lys Leu Leu
Lys Asp Ala Glu Ala Leu Ser 1400 1405	Gln Arg Leu Glu Glu 1410	Lys Ala Leu
Ala Tyr Asp Lys Leu Glu Lys 1415 1420	Thr Lys Asn Arg Leu 1425	Gln Gln Glu
Leu Asp Asp Leu Thr Val Asp 1430 1435	Leu Asp His Gln Arg 1440	Gln Val Ala

Ser Asn Leu Glu Lys Lys Gln Lys Lys Phe Asp Gln Leu Leu Ala  
 1445 1450 1455  
 Glu Glu Lys Ser Ile Ser Ala Arg Tyr Ala Glu Glu Arg Asp Arg  
 1460 1465 1470  
 Ala Glu Ala Glu Ala Arg Glu Lys Glu Thr Lys Ala Leu Ser Leu  
 1475 1480 1485  
 Ala Arg Ala Leu Glu Glu Ala Leu Glu Ala Lys Glu Glu Phe Glu  
 1490 1495 1500  
 Arg Gln Asn Lys Gln Leu Arg Ala Asp Met Glu Asp Leu Met Ser  
 1505 1510 1515  
 Ser Lys Asp Asp Val Gly Lys Asn Val His Glu Leu Glu Lys Ser  
 1520 1525 1530  
 Lys Arg Ala Leu Glu Gln Gln Val Glu Glu Met Arg Thr Gln Leu  
 1535 1540 1545  
 Glu Glu Leu Glu Asp Glu Leu Gln Ala Thr Glu Asp Ala Lys Leu  
 1550 1555 1560  
 Arg Leu Glu Val Asn Met Gln Ala Met Lys Ala Gln Phe Glu Arg  
 1565 1570 1575  
 Asp Leu Gln Thr Arg Asp Glu Gln Asn Glu Glu Lys Lys Arg Leu  
 1580 1585 1590  
 Leu Ile Lys Gln Val Arg Glu Leu Glu Ala Glu Leu Glu Asp Glu  
 1595 1600 1605  
 Arg Lys Gln Arg Ala Leu Ala Val Ala Ser Lys Lys Lys Met Glu  
 1610 1615 1620  
 Ile Asp Leu Lys Asp Leu Glu Ala Gln Ile Glu Ala Ala Asn Lys  
 1625 1630 1635  
 Ala Arg Asp Glu Val Ile Lys Gln Leu Arg Lys Leu Gln Ala Gln  
 1640 1645 1650  
 Met Lys Asp Tyr Gln Arg Glu Leu Glu Glu Ala Arg Ala Ser Arg  
 1655 1660 1665  
 Asp Glu Ile Phe Ala Gln Ser Lys Glu Ser Glu Lys Lys Leu Lys  
 1670 1675 1680  
 Ser Leu Glu Ala Glu Ile Leu Gln Leu Gln Glu Glu Leu Ala Ser  
 1685 1690 1695  
 Ser Glu Arg Ala Arg Arg His Ala Glu Gln Glu Arg Asp Glu Leu  
 1700 1705 1710  
 Ala Asp Glu Ile Thr Asn Ser Ala Ser Gly Lys Ser Ala Leu Leu  
 1715 1720 1725  
 Asp Glu Lys Arg Arg Leu Glu Ala Arg Ile Ala Gln Leu Glu Glu  
 1730 1735 1740

Glu Leu Glu Glu Glu Gln Ser Asn Met Glu Leu Leu Asn Asp Arg  
 1745 1750 1755  
 Phe Arg Lys Thr Thr Leu Gln Val Asp Thr Leu Asn Ala Glu Leu  
 1760 1765 1770  
 Ala Ala Glu Arg Ser Ala Ala Gln Lys Ser Asp Asn Ala Arg Gln  
 1775 1780 1785  
 Gln Leu Glu Arg Gln Asn Lys Glu Leu Lys Ala Lys Leu Gln Glu  
 1790 1795 1800  
 Leu Glu Gly Ala Val Lys Ser Lys Phe Lys Ala Thr Ile Ser Ala  
 1805 1810 1815  
 Leu Glu Ala Lys Ile Gly Gln Leu Glu Glu Gln Leu Glu Gln Glu  
 1820 1825 1830  
 Ala Lys Glu Arg Ala Ala Ala Asn Lys Leu Val Arg Arg Thr Glu  
 1835 1840 1845  
 Lys Lys Leu Lys Glu Ile Phe Met Gln Val Glu Asp Glu Arg Arg  
 1850 1855 1860  
 His Ala Asp Gln Tyr Lys Glu Gln Met Glu Lys Ala Asn Ala Arg  
 1865 1870 1875  
 Met Lys Gln Leu Lys Arg Gln Leu Glu Glu Ala Glu Glu Glu Ala  
 1880 1885 1890  
 Thr Arg Ala Asn Ala Ser Arg Arg Lys Leu Gln Arg Glu Leu Asp  
 1895 1900 1905  
 Asp Ala Thr Glu Ala Asn Glu Gly Leu Ser Arg Glu Val Ser Thr  
 1910 1915 1920  
 Leu Lys Asn Arg Leu Arg Arg Gly Gly Pro Ile Ser Phe Ser Ser  
 1925 1930 1935  
 Ser Arg Ser Gly Arg Arg Gln Leu His Leu Glu Gly Ala Ser Leu  
 1940 1945 1950  
 Glu Leu Ser Asp Asp Asp Thr Glu Ser Lys Thr Ser Asp Val Asn  
 1955 1960 1965  
 Glu Thr Gln Pro Pro Gln Ser Glu  
 1970 1975  
 <210> 158  
 <211> 1064  
 <212> PRT  
 <213> Homo sapiens  
 <400> 158  
 Met Lys Ile Ala Thr Val Ser Val Leu Leu Pro Leu Ala Leu Cys Leu  
 1 5 10 15  
 Ile Gln Asp Ala Ala Ser Lys Asn Glu Asp Gln Glu Met Cys His Glu  
 20 25 30

Phe Gln Ala Phe Met Lys Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys  
 35 40 45  
 Lys Phe Phe Gln Ser Leu Asp Gly Ile Met Phe Ile Asn Lys Cys Ala  
 50 55 60  
 Thr Cys Lys Met Ile Leu Glu Lys Glu Ala Lys Ser Gln Lys Arg Ala  
 65 70 75 80  
 Arg His Leu Ala Arg Ala Pro Lys Ala Thr Ala Pro Thr Glu Leu Asn  
 85 90 95  
 Cys Asp Asp Phe Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile Cys Pro  
 100 105 110  
 Asp Tyr Tyr Glu Ala Val Cys Gly Thr Asp Gly Lys Thr Tyr Asp Asn  
 115 120 125  
 Arg Cys Ala Leu Cys Ala Glu Asn Ala Lys Thr Gly Ser Gln Ile Gly  
 130 135 140  
 Val Lys Ser Glu Gly Glu Cys Lys Ser Ser Asn Pro Glu Gln Asp Val  
 145 150 155 160  
 Cys Ser Ala Phe Arg Pro Phe Val Arg Asp Gly Arg Leu Gly Cys Thr  
 165 170 175  
 Arg Glu Asn Asp Pro Val Leu Gly Pro Asp Gly Lys Thr His Gly Asn  
 180 185 190  
 Lys Cys Ala Met Cys Ala Glu Leu Phe Leu Lys Glu Ala Glu Asn Ala  
 195 200 205  
 Lys Arg Glu Gly Glu Thr Arg Ile Arg Arg Asn Ala Glu Lys Asp Phe  
 210 215 220  
 Cys Lys Glu Tyr Glu Lys Gln Val Arg Asn Gly Arg Leu Phe Cys Thr  
 225 230 235 240  
 Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Arg Met His Gly Asn  
 245 250 255  
 Lys Cys Ala Leu Cys Ala Glu Ile Phe Lys Arg Arg Phe Ser Glu Glu  
 260 265 270  
 Asn Ser Lys Thr Asp Gln Asn Leu Gly Lys Ala Glu Glu Lys Thr Lys  
 275 280 285  
 Val Lys Arg Glu Ile Val Lys Leu Cys Ser Gln Tyr Gln Asn Gln Ala  
 290 295 300  
 Lys Asn Gly Ile Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Arg Gly  
 305 310 315 320  
 Pro Asp Gly Lys Met His Gly Asn Leu Cys Ser Met Cys Gln Val Tyr  
 325 330 335  
 Phe Gln Ala Glu Asn Glu Glu Lys Lys Lys Ala Glu Ala Arg Ala Arg  
 340 345 350

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Asn Lys Arg Glu Ser Gly Lys Ala Thr Ser Tyr Ala Glu Leu Cys Asn
  355                      360                      365

Glu Tyr Arg Lys Leu Val Arg Asn Gly Lys Leu Ala Cys Thr Arg Glu
  370                      375                      380

Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Val His Gly Asn Thr Cys
  385                      390                      395                      400

Ser Met Cys Glu Val Phe Phe Gln Ala Glu Glu Glu Glu Lys Lys Lys
      405                      410                      415

Lys Glu Gly Glu Ser Arg Asn Lys Arg Gln Ser Lys Ser Thr Ala Ser
      420                      425                      430

Phe Glu Glu Leu Cys Ser Glu Tyr Arg Lys Ser Arg Lys Asn Gly Arg
      435                      440                      445

Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys
      450                      455                      460

Met His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln Gln Glu
      465                      470                      475                      480

Glu Arg Ala Arg Ala Lys Ala Lys Arg Glu Ala Ala Lys Glu Ile Cys
      485                      490                      495

Ser Glu Phe Arg Asp Gln Val Arg Asn Gly Thr Leu Ile Cys Thr Arg
      500                      505                      510

Glu His Asn Pro Val Arg Gly Pro Asp Gly Lys Met His Gly Asn Lys
      515                      520                      525

Cys Ala Met Cys Ala Ser Val Phe Lys Leu Glu Glu Glu Glu Lys Lys
      530                      535                      540

Asn Asp Lys Glu Glu Lys Gly Lys Val Glu Ala Glu Lys Val Lys Arg
      545                      550                      555                      560

Glu Ala Val Gln Glu Leu Cys Ser Glu Tyr Arg His Tyr Val Arg Asn
      565                      570                      575

Gly Arg Leu Pro Cys Thr Arg Glu Asn Asp Pro Ile Glu Gly Leu Asp
      580                      585                      590

Gly Lys Ile His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln
      595                      600                      605

Gln Glu Ala Lys Glu Lys Glu Arg Ala Glu Pro Arg Ala Lys Val Lys
      610                      615                      620

Arg Glu Ala Glu Lys Glu Thr Cys Asp Glu Phe Arg Arg Leu Leu Gln
      625                      630                      635                      640

Asn Gly Lys Leu Phe Cys Thr Arg Glu Asn Asp Pro Val Arg Gly Pro
      645                      650                      655

Asp Gly Lys Thr His Gly Asn Lys Cys Ala Met Cys Lys Ala Val Phe

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660	665	670
Gln Lys Glu Asn Glu Glu Arg Lys Arg Lys Glu Glu Glu Asp Gln Arg 675 680 685		
Asn Ala Ala Gly His Gly Ser Ser Gly Gly Gly Gly Gly Asn Thr Gln 690 695 700		
Asp Glu Cys Ala Glu Tyr Gln Glu Gln Met Lys Asn Gly Arg Leu Ser 705 710 715 720		
Cys Thr Arg Glu Ser Asp Pro Val Arg Asp Ala Asp Gly Lys Ser Tyr 725 730 735		
Asn Asn Gln Cys Thr Met Cys Lys Ala Lys Leu Glu Arg Glu Ala Glu 740 745 750		
Arg Lys Asn Glu Tyr Ser Arg Ser Arg Ser Asn Gly Thr Gly Ser Glu 755 760 765		
Ser Gly Lys Asp Thr Cys Asp Glu Phe Arg Ser Gln Met Lys Asn Gly 770 775 780		
Lys Leu Ile Cys Thr Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly 785 790 795 800		
Lys Thr His Gly Asn Lys Cys Thr Met Cys Lys Glu Lys Leu Glu Arg 805 810 815		
Glu Ala Ala Glu Lys Lys Lys Lys Glu Asp Glu Asp Arg Ser Asn Thr 820 825 830		
Gly Glu Arg Ser Asn Thr Gly Glu Arg Ser Asn Asp Lys Glu Asp Leu 835 840 845		
Cys Arg Glu Phe Arg Ser Met Gln Arg Asn Gly Lys Leu Ile Cys Thr 850 855 860		
Arg Glu Asn Asn Pro Val Arg Gly Pro Tyr Gly Lys Met His Ile Asn 865 870 875 880		
Lys Cys Ala Met Cys Gln Ser Ile Phe Asp Arg Glu Ala Asn Glu Arg 885 890 895		
Lys Lys Lys Asp Glu Glu Lys Ser Ser Ser Lys Pro Ser Asn Asn Ala 900 905 910		
Lys Asp Glu Cys Ser Glu Phe Arg Asn Tyr Ile Arg Asn Asn Glu Leu 915 920 925		
Ile Cys Pro Arg Glu Asn Asp Pro Val His Gly Ala Asp Gly Lys Phe 930 935 940		
Tyr Thr Asn Lys Cys Tyr Met Cys Arg Ala Val Phe Leu Thr Glu Ala 945 950 955 960		
Leu Glu Arg Ala Lys Leu Gln Glu Lys Pro Ser His Val Arg Ala Ser 965 970 975		

Gln Glu Glu Asp Ser Pro Asp Ser Phe Ser Ser Leu Asp Ser Glu Met  
 980 985 990

Cys Lys Asp Tyr Arg Val Leu Pro Arg Ile Gly Tyr Leu Cys Pro Lys  
 995 1000 1005

Asp Leu Lys Pro Val Cys Gly Asp Asp Gly Gln Thr Tyr Asn Asn  
 1010 1015 1020

Pro Cys Met Leu Cys His Glu Asn Leu Ile Arg Gln Thr Asn Thr  
 1025 1030 1035

His Ile Arg Ser Thr Gly Lys Cys Glu Glu Ser Ser Thr Pro Gly  
 1040 1045 1050

Thr Thr Ala Ala Ser Met Pro Pro Ser Asp Glu  
 1055 1060

<210> 159  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 159

Met His Lys Glu Glu His Glu Val Ala Val Leu Gly Ala Pro Pro Ser  
 1 5 10 15

Thr Ile Leu Pro Arg Ser Thr Val Ile Asn Ile His Ser Glu Thr Ser  
 20 25 30

Val Pro Asp His Val Val Trp Ser Leu Phe Asn Thr Leu Phe Leu Asn  
 35 40 45

Trp Cys Cys Leu Gly Phe Ile Ala Phe Ala Tyr Ser Val Lys Ser Arg  
 50 55 60

Asp Arg Lys Met Val Gly Asp Val Thr Gly Ala Gln Ala Tyr Ala Ser  
 65 70 75 80

Thr Ala Lys Cys Leu Asn Ile Trp Ala Leu Ile Leu Gly Ile Leu Met  
 85 90 95

Thr Ile Gly Phe Ile Leu Leu Leu Val Phe Gly Ser Val Thr Val Tyr  
 100 105 110

His Ile Met Leu Gln Ile Ile Gln Glu Lys Arg Gly Tyr  
 115 120 125

<210> 160  
 <211> 400  
 <212> PRT  
 <213> Homo sapiens

<400> 160

Met Met Asp Leu Arg Asn Thr Pro Ala Lys Ser Leu Asp Lys Phe Ile  
 1 5 10 15

Glu Asp Tyr Leu Leu Pro Asp Thr Cys Phe Arg Met Gln Ile Asp His  
 20 25 30

Ala Ile Asp Ile Ile Cys Gly Phe Leu Lys Glu Arg Cys Phe Arg Gly

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          35              40              45

Ser Ser Tyr Pro Val Cys Val Ser Lys Val Val Lys Gly Gly Ser Ser
 50                    55                    60

Gly Lys Gly Thr Thr Leu Arg Gly Arg Ser Asp Ala Asp Leu Val Val
65                    70                    75                    80

Phe Leu Ser Pro Leu Thr Thr Phe Gln Asp Gln Leu Asn Arg Arg Gly
      85                    90                    95

Glu Phe Ile Gln Glu Ile Arg Arg Gln Leu Glu Ala Cys Gln Arg Glu
      100                    105                    110

Arg Ala Leu Ser Val Lys Phe Glu Val Gln Ala Pro Arg Trp Gly Asn
      115                    120                    125

Pro Arg Ala Leu Ser Phe Val Leu Ser Ser Leu Gln Leu Gly Glu Gly
      130                    135                    140

Val Glu Phe Asp Val Leu Pro Ala Phe Asp Ala Leu Gly Gln Leu Thr
145                    150                    155                    160

Gly Ser Tyr Lys Pro Asn Pro Gln Ile Tyr Val Lys Leu Ile Glu Glu
      165                    170                    175

Cys Thr Asp Leu Gln Lys Glu Gly Glu Phe Ser Thr Cys Phe Thr Glu
      180                    185                    190

Leu Gln Arg Asp Phe Leu Lys Gln Arg Pro Thr Lys Leu Lys Ser Leu
      195                    200                    205

Ile Arg Leu Val Lys His Trp Tyr Gln Asn Cys Lys Lys Lys Leu Gly
      210                    215                    220

Lys Leu Pro Pro Gln Tyr Ala Leu Glu Leu Leu Thr Val Tyr Ala Trp
225                    230                    235                    240

Glu Arg Gly Ser Met Lys Thr His Phe Asn Thr Ala Gln Gly Phe Arg
      245                    250                    255

Thr Val Leu Glu Leu Val Ile Asn Tyr Gln Gln Leu Cys Ile Tyr Trp
      260                    265                    270

Thr Lys Tyr Tyr Asp Phe Lys Asn Pro Ile Ile Glu Lys Tyr Leu Arg
      275                    280                    285

Arg Gln Leu Thr Lys Pro Arg Pro Val Ile Leu Asp Pro Ala Asp Pro
      290                    295                    300

Thr Gly Asn Leu Gly Gly Gly Asp Pro Lys Gly Trp Arg Gln Leu Ala
305                    310                    315                    320

Gln Glu Ala Glu Ala Trp Leu Asn Tyr Pro Cys Phe Lys Asn Trp Asp
      325                    330                    335

Gly Ser Pro Val Ser Ser Trp Ile Leu Leu Ala Glu Ser Asn Ser Thr
      340                    345                    350

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Asp Asp Glu Thr Asp Asp Pro Arg Thr Tyr Gln Lys Tyr Gly Tyr Ile  
355 360 365

Gly Thr His Glu Tyr Pro His Phe Ser His Arg Pro Ser Thr Leu Gln  
370 375 380

Ala Ala Ser Thr Pro Gln Ala Glu Glu Asp Trp Thr Cys Thr Ile Leu  
385 390 395 400

<210> 161  
<211> 370  
<212> PRT  
<213> Homo sapiens

<400> 161

Met Glu Asn Gln Val Leu Thr Pro His Val Tyr Trp Ala Gln Arg His  
1 5 10 15

Arg Glu Leu Tyr Leu Arg Val Glu Leu Ser Asp Val Gln Asn Pro Ala  
20 25 30

Ile Ser Ile Thr Glu Asn Val Leu His Phe Lys Ala Gln Gly His Gly  
35 40 45

Ala Lys Gly Asp Asn Val Tyr Glu Phe His Leu Glu Phe Leu Asp Leu  
50 55 60

Val Lys Pro Glu Pro Val Tyr Lys Leu Thr Gln Arg Gln Val Asn Ile  
65 70 75 80

Thr Val Gln Lys Lys Val Ser Gln Trp Trp Glu Arg Leu Thr Lys Gln  
85 90 95

Glu Lys Arg Pro Leu Phe Leu Ala Pro Asp Phe Asp Arg Trp Leu Asp  
100 105 110

Glu Ser Asp Ala Glu Met Glu Leu Arg Ala Lys Glu Glu Glu Arg Leu  
115 120 125

Asn Lys Leu Arg Leu Glu Ser Glu Gly Ser Pro Glu Thr Leu Thr Asn  
130 135 140

Leu Arg Lys Gly Tyr Leu Phe Met Tyr Asn Leu Val Gln Phe Leu Gly  
145 150 155 160

Phe Ser Trp Ile Phe Val Asn Leu Thr Val Arg Phe Cys Ile Leu Gly  
165 170 175

Lys Glu Ser Phe Tyr Asp Thr Phe His Thr Val Ala Asp Met Met Tyr  
180 185 190

Phe Cys Gln Met Leu Ala Val Val Glu Thr Ile Asn Ala Ala Ile Gly  
195 200 205

Val Thr Thr Ser Pro Val Leu Pro Ser Leu Ile Gln Leu Leu Gly Arg  
210 215 220

Asn Phe Ile Leu Phe Ile Ile Phe Gly Thr Met Glu Glu Met Gln Asn  
225 230 235 240

Lys Ala Val Val Phe Phe Val Phe Tyr Leu Trp Ser Ala Ile Glu Ile  
245 250 255

Phe Arg Tyr Ser Phe Tyr Met Leu Thr Cys Ile Asp Met Asp Trp Lys  
260 265 270

Val Leu Thr Trp Leu Arg Tyr Thr Leu Trp Ile Pro Leu Tyr Pro Leu  
275 280 285

Gly Cys Leu Ala Glu Ala Val Ser Val Ile Gln Ser Ile Pro Ile Phe  
290 295 300

Asn Glu Thr Gly Arg Phe Ser Phe Thr Leu Pro Tyr Pro Val Lys Ile  
305 310 315 320

Lys Val Arg Phe Ser Phe Phe Leu Gln Ile Tyr Leu Ile Met Ile Phe  
325 330 335

Leu Gly Leu Tyr Ile Asn Phe Arg His Leu Tyr Lys Gln Arg Arg Leu  
340 345 350

Lys Met Arg Ala Gly Ala Val Ala His Ala Cys Asp Pro Ser Ala Leu  
355 360 365

Gly Gly  
370

<210> 162  
<211> 372  
<212> PRT  
<213> Homo sapiens

<400> 162

Met Leu Asp Gly Leu Gly Val Val Ala Ile Ser Ile Phe Gly Ile Gln  
1 5 10 15

Leu Lys Thr Glu Gly Ser Leu Arg Thr Ala Val Pro Gly Ile Pro Thr  
20 25 30

Gln Ser Ala Phe Asn Lys Cys Leu Gln Arg Tyr Ile Gly Ala Leu Gly  
35 40 45

Ala Arg Val Ile Cys Asp Asn Ile Pro Gly Leu Val Ser Arg Gln Arg  
50 55 60

Gln Leu Cys Gln Arg Tyr Pro Asp Ile Met Arg Ser Val Gly Glu Gly  
65 70 75 80

Ala Arg Glu Trp Ile Arg Glu Cys Gln His Gln Phe Arg His His Arg  
85 90 95

Trp Asn Cys Thr Thr Leu Asp Arg Asp His Thr Val Phe Gly Arg Val  
100 105 110

Met Leu Arg Ser Ser Arg Glu Ala Ala Phe Val Tyr Ala Ile Ser Ser  
115 120 125

Ala Gly Val Ile His Ala Ile Thr Arg Ala Cys Ser Gln Gly Glu Leu  
130 135 140

Ser Val Cys Ser Cys Asp Pro Tyr Thr Arg Gly Arg His His Asp Gln  
 145 150 155 160  
 Arg Gly Thr Phe Asp Trp Gly Gly Cys Ser Asp Asn Ile His Tyr Gly  
 165 170 175  
 Val Arg Phe Ala Lys Ala Phe Val Asp Ala Lys Glu Lys Arg Leu Lys  
 180 185 190  
 Asp Ala Arg Ala Leu Met Asn Leu His Asn Asn Arg Cys Gly Arg Thr  
 195 200 205  
 Ala Val Arg Arg Phe Val Lys Leu Glu Cys Lys Cys His Gly Val Ser  
 210 215 220  
 Gly Ser Cys Thr Leu Arg Thr Cys Trp Arg Ala Leu Ser Asp Phe Arg  
 225 230 235 240  
 Arg Thr Gly Asp Tyr Leu Arg Arg Arg Tyr Asp Gly Ala Val Gln Val  
 245 250 255  
 Met Ala Thr Gln Asp Gly Ala Asn Phe Thr Ala Ala Arg Gln Gly Tyr  
 260 265 270  
 Arg Arg Ala Thr Arg Ser Asp Leu Val Tyr Phe Asp Asn Ser Pro Asp  
 275 280 285  
 Tyr Cys Val Leu Asp Lys Ala Ala Gly Ser Leu Gly Thr Ala Gly Arg  
 290 295 300  
 Val Cys Ser Lys Thr Ser Lys Gly Thr Asp Gly Cys Glu Ile Met Cys  
 305 310 315 320  
 Cys Gly Arg Gly Tyr Asp Thr Thr Arg Val Thr Arg Val Thr Gln Cys  
 325 330 335  
 Glu Cys Lys Phe His Trp Cys Cys Ala Val Arg Cys Lys Glu Cys Arg  
 340 345 350  
 Asn Thr Val Asp Val His Thr Cys Lys Ala Pro Lys Lys Ala Glu Trp  
 355 360 365  
 Leu Asp Gln Thr  
 370

<210> 163  
 <211> 249  
 <212> PRT  
 <213> Homo sapiens

<400> 163

Met Lys Leu Asn Ile Ser Phe Pro Ala Thr Gly Cys Gln Lys Leu Ile  
 1 5 10 15  
 Glu Val Asp Asp Glu Arg Thr Leu Arg Thr Phe Tyr Glu Lys Arg Met  
 20 25 30  
 Ala Thr Glu Val Ala Ala Asp Ala Leu Gly Glu Glu Trp Lys Gly Tyr  
 35 40 45

Val Val Arg Ile Ser Gly Gly Asn Asp Lys Gln Gly Phe Pro Met Lys  
50 55 60

Gln Gly Val Leu Thr His Gly Arg Val Arg Leu Leu Leu Ser Lys Gly  
65 70 75 80

His Ser Cys Tyr Arg Pro Arg Arg Thr Gly Glu Arg Lys Arg Lys Ser  
85 90 95

Val Arg Gly Cys Ile Val Asp Ala Asn Leu Ser Val Leu Asn Leu Val  
100 105 110

Ile Val Lys Lys Gly Glu Lys Asp Ile Pro Gly Leu Thr Asp Thr Thr  
115 120 125

Val Pro Arg Arg Leu Gly Pro Lys Arg Ala Ser Arg Ile Arg Lys Arg  
130 135 140

Phe Asn Leu Ser Lys Glu Asp Asp Val Arg Gln Tyr Val Val Arg Lys  
145 150 155 160

Pro Leu Asn Lys Glu Gly Lys Lys Pro Arg Thr Lys Ala Pro Lys Ile  
165 170 175

Gln Arg Leu Val Thr Pro Arg Val Leu Gln His Lys Arg Arg Arg Ile  
180 185 190

Ala Leu Lys Gln Gln Arg Thr Lys Lys Asn Lys Glu Glu Ala Ala Glu  
195 200 205

Tyr Ala Lys Leu Leu Ala Lys Arg Met Lys Glu Ala Lys Glu Lys Arg  
210 215 220

Gln Glu Gln Ile Ala Lys Arg Arg Arg Leu Ser Ser Leu Arg Ala Ser  
225 230 235 240

Thr Ser Lys Ser Glu Ser Ser Gln Lys  
245

<210> 164  
<211> 469  
<212> PRT  
<213> Homo sapiens

<400> 164

Met His Ser Phe Pro Pro Leu Leu Leu Leu Phe Trp Gly Val Val  
1 5 10 15

Ser His Ser Phe Pro Ala Thr Leu Glu Thr Gln Glu Gln Asp Val Asp  
20 25 30

Leu Val Gln Lys Tyr Leu Glu Lys Tyr Tyr Asn Leu Lys Asn Asp Gly  
35 40 45

Arg Gln Val Glu Lys Arg Arg Asn Ser Gly Pro Val Val Glu Lys Leu  
50 55 60

Lys Gln Met Gln Glu Phe Phe Gly Leu Lys Val Thr Gly Lys Pro Asp  
65 70 75 80

Ala Glu Thr Leu Lys Val Met Lys Gln Pro Arg Cys Gly Val Pro Asp  
 85 90 95  
 Val Ala Gln Phe Val Leu Thr Glu Gly Asn Pro Arg Trp Glu Gln Thr  
 100 105 110  
 His Leu Thr Tyr Arg Ile Glu Asn Tyr Thr Pro Asp Leu Pro Arg Ala  
 115 120 125  
 Asp Val Asp His Ala Ile Glu Lys Ala Phe Gln Leu Trp Ser Asn Val  
 130 135 140  
 Thr Pro Leu Thr Phe Thr Lys Val Ser Glu Gly Gln Ala Asp Ile Met  
 145 150 155 160  
 Ile Ser Phe Val Arg Gly Asp His Arg Asp Asn Ser Pro Phe Asp Gly  
 165 170 175  
 Pro Gly Gly Asn Leu Ala His Ala Phe Gln Pro Gly Pro Gly Ile Gly  
 180 185 190  
 Gly Asp Ala His Phe Asp Glu Asp Glu Arg Trp Thr Asn Asn Phe Arg  
 195 200 205  
 Glu Tyr Asn Leu His Arg Val Ala Ala His Glu Leu Gly His Ser Leu  
 210 215 220  
 Gly Leu Ser His Ser Thr Asp Ile Gly Ala Leu Met Tyr Pro Ser Tyr  
 225 230 235 240  
 Thr Phe Ser Gly Asp Val Gln Leu Ala Gln Asp Asp Ile Asp Gly Ile  
 245 250 255  
 Gln Ala Ile Tyr Gly Arg Ser Gln Asn Pro Val Gln Pro Ile Gly Pro  
 260 265 270  
 Gln Thr Pro Lys Ala Cys Asp Ser Lys Leu Thr Phe Asp Ala Ile Thr  
 275 280 285  
 Thr Ile Arg Gly Glu Val Met Phe Phe Lys Asp Arg Phe Tyr Met Arg  
 290 295 300  
 Thr Asn Pro Phe Tyr Pro Glu Val Glu Leu Asn Phe Ile Ser Val Phe  
 305 310 315 320  
 Trp Pro Gln Leu Pro Asn Gly Leu Glu Ala Ala Tyr Glu Phe Ala Asp  
 325 330 335  
 Arg Asp Glu Val Arg Phe Phe Lys Gly Asn Lys Tyr Trp Ala Val Gln  
 340 345 350  
 Gly Gln Asn Val Leu His Gly Tyr Pro Lys Asp Ile Tyr Ser Ser Phe  
 355 360 365  
 Gly Phe Pro Arg Thr Val Lys His Ile Asp Ala Ala Leu Ser Glu Glu  
 370 375 380  
 Asn Thr Gly Lys Thr Tyr Phe Phe Val Ala Asn Lys Tyr Trp Arg Tyr  
 385 390 395 400

Asp Glu Tyr Lys Arg Ser Met Asp Pro Gly Tyr Pro Lys Met Ile Ala  
405 410 415

His Asp Phe Pro Gly Ile Gly His Lys Val Asp Ala Val Phe Met Lys  
420 425 430

Asp Gly Phe Phe Tyr Phe Phe His Gly Thr Arg Gln Tyr Lys Phe Asp  
435 440 445

Pro Lys Thr Lys Arg Ile Leu Thr Leu Gln Lys Ala Asn Ser Trp Phe  
450 455 460

Asn Cys Arg Lys Asn  
465

<210> 165  
<211> 156  
<212> PRT  
<213> Homo sapiens

<400> 165

Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu  
1 5 10 15

Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp  
20 25 30

Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys  
35 40 45

Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu  
50 55 60

Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Ala Lys Lys Arg  
65 70 75 80

Lys Lys Lys Ser Tyr Thr Thr Pro Lys Lys Asn Lys His Lys Arg Lys  
85 90 95

Lys Val Lys Leu Ala Val Leu Lys Tyr Tyr Lys Val Asp Glu Asn Gly  
100 105 110

Lys Ile Ser Arg Leu Arg Arg Glu Cys Pro Ser Asp Glu Cys Gly Ala  
115 120 125

Gly Val Phe Met Ala Ser His Phe Asp Arg His Tyr Cys Gly Lys Cys  
130 135 140

Cys Leu Thr Tyr Cys Phe Asn Lys Pro Glu Asp Lys  
145 150 155

<210> 166  
<211> 783  
<212> PRT  
<213> Homo sapiens

<400> 166

Met Ala Lys Tyr Asn Thr Gly Gly Asn Pro Thr Glu Asp Val Ser Val  
1 5 10 15

Asn Ser Arg Pro Phe Arg Val Thr Gly Pro Asn Ser Ser Ser Gly Ile  
 20 25 30  
 Gln Ala Arg Lys Asn Leu Phe Asn Asn Gln Gly Asn Ala Ser Pro Pro  
 35 40 45  
 Ala Gly Pro Ser Asn Val Pro Lys Phe Gly Ser Pro Lys Pro Pro Val  
 50 55 60  
 Ala Val Lys Pro Ser Ser Glu Glu Lys Pro Asp Lys Glu Pro Lys Pro  
 65 70 75 80  
 Pro Phe Leu Lys Pro Thr Gly Ala Gly Gln Arg Phe Gly Thr Pro Ala  
 85 90 95  
 Ser Leu Thr Thr Arg Asp Pro Glu Ala Lys Val Gly Phe Leu Lys Pro  
 100 105 110  
 Val Gly Pro Lys Pro Ile Asn Leu Pro Lys Glu Asp Ser Lys Pro Thr  
 115 120 125  
 Phe Pro Trp Pro Pro Gly Asn Lys Pro Ser Leu His Ser Val Asn Gln  
 130 135 140  
 Asp His Asp Leu Lys Pro Leu Gly Pro Lys Ser Gly Pro Thr Pro Pro  
 145 150 155 160  
 Thr Ser Glu Asn Glu Gln Lys Gln Ala Phe Pro Lys Leu Thr Gly Val  
 165 170 175  
 Lys Gly Lys Phe Met Ser Ala Ser Gln Asp Leu Glu Pro Lys Pro Leu  
 180 185 190  
 Phe Pro Lys Pro Ala Phe Gly Gln Lys Pro Pro Leu Ser Thr Glu Asn  
 195 200 205  
 Ser His Glu Asp Glu Ser Pro Met Lys Asn Val Ser Ser Ser Lys Gly  
 210 215 220  
 Ser Pro Ala Pro Leu Gly Val Arg Ser Lys Ser Gly Pro Leu Lys Pro  
 225 230 235 240  
 Ala Arg Glu Asp Ser Glu Asn Lys Asp His Ala Gly Glu Ile Ser Ser  
 245 250 255  
 Leu Pro Phe Pro Gly Val Val Leu Lys Pro Ala Ala Ser Arg Gly Gly  
 260 265 270  
 Leu Gly Leu Ser Lys Asn Gly Glu Glu Lys Lys Glu Asp Arg Lys Ile  
 275 280 285  
 Asp Ala Ala Lys Asn Thr Phe Gln Ser Lys Ile Asn Gln Glu Glu Leu  
 290 295 300  
 Ala Ser Gly Thr Pro Pro Ala Arg Phe Pro Lys Ala Pro Ser Lys Leu  
 305 310 315 320  
 Thr Val Gly Gly Pro Trp Gly Gln Ser Gln Glu Lys Glu Lys Gly Asp  
 325 330 335

Lys Asn Ser Ala Thr Pro Lys Gln Lys Pro Leu Pro Pro Leu Phe Thr  
 340 345 350  
 Leu Gly Pro Pro Pro Pro Lys Pro Asn Arg Pro Pro Asn Val Asp Leu  
 355 360 365  
 Thr Lys Phe His Lys Thr Ser Ser Gly Asn Ser Thr Ser Lys Gly Gln  
 370 375 380  
 Thr Ser Tyr Ser Thr Thr Ser Leu Pro Pro Pro Pro Pro Ser His Pro  
 385 390 395 400  
 Ala Ser Gln Pro Pro Leu Pro Ala Ser His Pro Ser Gln Pro Pro Val  
 405 410 415  
 Pro Ser Leu Pro Pro Arg Asn Ile Lys Pro Pro Phe Asp Leu Lys Ser  
 420 425 430  
 Pro Val Asn Glu Asp Asn Gln Asp Gly Val Thr His Ser Asp Gly Ala  
 435 440 445  
 Gly Asn Leu Asp Glu Glu Gln Asp Ser Glu Gly Glu Thr Tyr Glu Asp  
 450 455 460  
 Ile Glu Ala Ser Lys Glu Arg Glu Lys Lys Arg Glu Lys Glu Glu Lys  
 465 470 475 480  
 Lys Arg Leu Glu Leu Glu Lys Lys Glu Gln Lys Glu Lys Glu Lys Lys  
 485 490 495  
 Glu Gln Glu Ile Lys Lys Lys Phe Lys Leu Thr Gly Pro Ile Gln Val  
 500 505 510  
 Ile His Leu Ala Lys Ala Cys Cys Asp Val Lys Gly Gly Lys Asn Glu  
 515 520 525  
 Leu Ser Phe Lys Gln Gly Glu Gln Ile Glu Ile Ile Arg Ile Thr Asp  
 530 535 540  
 Asn Pro Glu Gly Lys Trp Leu Gly Arg Thr Ala Arg Gly Ser Tyr Gly  
 545 550 555 560  
 Tyr Ile Lys Thr Thr Ala Val Glu Ile Asp Tyr Asp Ser Leu Lys Leu  
 565 570 575  
 Lys Lys Asp Ser Leu Gly Ala Pro Ser Arg Pro Ile Glu Asp Asp Gln  
 580 585 590  
 Glu Val Tyr Asp Asp Val Ala Glu Gln Asp Asp Ile Ser Ser His Ser  
 595 600 605  
 Gln Ser Gly Ser Gly Gly Ile Phe Pro Pro Pro Pro Asp Asp Asp Ile  
 610 615 620  
 Tyr Asp Gly Ile Glu Glu Glu Asp Ala Asp Asp Gly Phe Pro Ala Pro  
 625 630 635 640  
 Pro Lys Gln Leu Asp Met Gly Asp Glu Val Tyr Asp Asp Val Asp Thr  
 645 650 655



Ser Asp Phe Pro Val Ser Ser Ala Glu Met Ser Gln Gly Thr Asn Phe  
660 665 670

Gly Lys Ala Lys Thr Glu Glu Lys Asp Leu Lys Lys Leu Lys Lys Gln  
675 680 685

Glu Lys Glu Glu Lys Asp Phe Arg Lys Lys Phe Lys Tyr Asp Gly Glu  
690 695 700

Ile Arg Val Leu Tyr Ser Thr Lys Val Thr Thr Ser Ile Thr Ser Lys  
705 710 715 720

Lys Trp Gly Thr Arg Asp Leu Gln Val Lys Pro Gly Glu Ser Leu Glu  
725 730 735

Val Ile Gln Thr Thr Asp Asp Thr Lys Val Leu Cys Arg Asn Glu Glu  
740 745 750

Gly Lys Tyr Gly Tyr Val Leu Arg Ser Tyr Leu Ala Asp Asn Asp Gly  
755 760 765

Glu Ile Tyr Asp Asp Ile Ala Asp Gly Cys Ile Tyr Asp Asn Asp  
770 775 780

<210> 167  
<211> 117  
<212> PRT  
<213> Homo sapiens

<400> 167

Met Ala Ala Ala Ala Ala Gly Ser Gly Thr Pro Arg Glu Glu Glu  
1 5 10 15

Val Pro Ala Gly Glu Ala Ala Ala Ser Gln Pro Gln Ala Pro Thr Ser  
20 25 30

Val Pro Gly Ala Arg Leu Ser Arg Leu Pro Leu Ala Arg Val Lys Ala  
35 40 45

Leu Val Lys Ala Asp Pro Asp Val Thr Leu Ala Gly Gln Glu Ala Ile  
50 55 60

Phe Ile Leu Ala Arg Ala Ala Glu Leu Phe Val Glu Thr Ile Ala Lys  
65 70 75 80

Asp Ala Tyr Cys Cys Ala Gln Gln Gly Lys Arg Lys Thr Leu Gln Arg  
85 90 95

Arg Asp Leu Asp Asn Ala Ile Glu Ala Val Asp Glu Phe Ala Phe Leu  
100 105 110

Glu Gly Thr Leu Asp  
115

<210> 168  
<211> 243  
<212> PRT  
<213> Homo sapiens

<400> 168

Met Ala Val Gln Ile Ser Lys Arg Arg Lys Phe Val Ala Asp Gly Ile  
 1 5 10 15  
 Phe Lys Ala Glu Leu Asn Glu Phe Leu Thr Arg Glu Leu Ala Glu Asp  
 20 25 30  
 Gly Tyr Ser Gly Val Glu Val Arg Val Thr Pro Thr Arg Thr Glu Ile  
 35 40 45  
 Ile Ile Leu Ala Thr Arg Thr Gln Asn Val Leu Gly Glu Lys Gly Arg  
 50 55 60  
 Arg Ile Arg Glu Leu Thr Ala Val Val Gln Lys Arg Phe Gly Phe Pro  
 65 70 75 80  
 Glu Gly Ser Val Glu Leu Tyr Ala Glu Lys Val Ala Thr Arg Gly Leu  
 85 90 95  
 Cys Ala Ile Ala Gln Ala Glu Ser Leu Arg Tyr Lys Leu Leu Gly Gly  
 100 105 110  
 Leu Ala Val Arg Arg Ala Cys Tyr Gly Val Leu Arg Phe Ile Met Glu  
 115 120 125  
 Ser Gly Ala Lys Gly Cys Glu Val Val Val Ser Gly Lys Leu Arg Gly  
 130 135 140  
 Gln Arg Ala Lys Ser Met Lys Phe Val Asp Gly Leu Met Ile His Ser  
 145 150 155 160  
 Gly Asp Pro Val Asn Tyr Tyr Val Asp Thr Ala Val Arg His Val Leu  
 165 170 175  
 Leu Arg Gln Gly Val Leu Gly Ile Lys Val Lys Ile Met Leu Pro Trp  
 180 185 190  
 Asp Pro Thr Gly Lys Ile Gly Pro Lys Lys Pro Leu Pro Asp His Val  
 195 200 205  
 Ser Ile Val Glu Pro Lys Asp Glu Ile Leu Pro Thr Thr Pro Ile Ser  
 210 215 220  
 Glu Gln Lys Gly Gly Lys Pro Glu Pro Pro Ala Met Pro Gln Pro Val  
 225 230 235 240  
 Pro Thr Ala

<210> 169  
 <211> 136  
 <212> PRT  
 <213> Homo sapiens

<400> 169

Met Val Leu Leu Glu Ser Glu Gln Phe Leu Thr Glu Leu Thr Arg Leu  
 1 5 10 15  
 Phe Gln Lys Cys Arg Thr Ser Gly Ser Val Tyr Ile Thr Leu Lys Lys  
 20 25 30

Tyr Asp Gly Arg Thr Lys Pro Ile Pro Lys Lys Gly Thr Val Glu Gly  
 35 40 45  
 Phe Glu Pro Ala Asp Asn Lys Cys Leu Leu Arg Ala Thr Asp Gly Lys  
 50 55 60  
 Lys Lys Ile Ser Thr Val Val Ser Ser Lys Glu Val Asn Lys Phe Gln  
 65 70 75 80  
 Met Ala Tyr Ser Asn Leu Leu Arg Ala Asn Met Asp Gly Leu Lys Lys  
 85 90 95  
 Arg Asp Lys Lys Asn Lys Thr Lys Lys Thr Lys Ala Ala Ala Ala Ala  
 100 105 110  
 Ala Ala Ala Ala Pro Ala Ala Ala Thr Ala Ala Thr Thr Ala Ala  
 115 120 125  
 Thr Thr Ala Ala Thr Ala Ala Gln  
 130 135  
 <210> 170  
 <211> 409  
 <212> PRT  
 <213> Homo sapiens  
 <400> 170  
 Met Gln Val Thr Leu Lys Thr Leu Gln Gln Gln Thr Phe Lys Ile Asp  
 1 5 10 15  
 Ile Asp Pro Glu Glu Thr Val Lys Ala Leu Lys Glu Lys Ile Glu Ser  
 20 25 30  
 Glu Lys Gly Lys Asp Ala Phe Pro Val Ala Gly Gln Lys Leu Ile Tyr  
 35 40 45  
 Ala Gly Lys Ile Leu Asn Asp Asp Thr Ala Leu Lys Glu Tyr Lys Ile  
 50 55 60  
 Asp Glu Lys Asn Phe Val Val Val Met Val Thr Lys Pro Lys Ala Val  
 65 70 75 80  
 Ser Thr Pro Ala Pro Ala Thr Thr Gln Gln Ser Ala Pro Ala Ser Thr  
 85 90 95  
 Thr Ala Val Thr Ser Ser Thr Thr Thr Thr Val Ala Gln Ala Pro Thr  
 100 105 110  
 Pro Val Pro Ala Leu Ala Pro Thr Ser Thr Pro Ala Ser Ile Thr Pro  
 115 120 125  
 Ala Ser Ala Thr Ala Ser Ser Glu Pro Ala Pro Ala Ser Ala Ala Lys  
 130 135 140  
 Gln Glu Lys Pro Ala Glu Lys Pro Ala Glu Thr Pro Val Ala Thr Ser  
 145 150 155 160  
 Pro Thr Ala Thr Asp Ser Thr Ser Gly Asp Ser Ser Arg Ser Asn Leu  
 165 170 175

Phe Glu Asp Ala Thr Ser Ala Leu Val Thr Gly Gln Ser Tyr Glu Asn  
 180 185 190  
 Met Val Thr Glu Ile Met Ser Met Gly Tyr Glu Arg Glu Gln Val Ile  
 195 200 205  
 Ala Ala Leu Arg Ala Ser Phe Asn Asn Pro Asp Arg Ala Val Glu Tyr  
 210 215 220  
 Leu Leu Met Gly Ile Pro Gly Asp Arg Glu Ser Gln Ala Val Val Asp  
 225 230 235 240  
 Pro Pro Gln Ala Ala Ser Thr Gly Ala Pro Gln Ser Ser Ala Val Ala  
 245 250 255  
 Ala Ala Ala Ala Thr Thr Thr Ala Thr Thr Thr Thr Thr Ser Ser Gly  
 260 265 270  
 Gly His Pro Leu Glu Phe Leu Arg Asn Gln Pro Gln Phe Gln Gln Met  
 275 280 285  
 Arg Gln Ile Ile Gln Gln Asn Pro Ser Leu Leu Pro Ala Leu Leu Gln  
 290 295 300  
 Gln Ile Gly Arg Glu Asn Pro Gln Leu Leu Gln Gln Ile Ser Gln His  
 305 310 315 320  
 Gln Glu His Phe Ile Gln Met Leu Asn Glu Pro Val Gln Glu Ala Gly  
 325 330 335  
 Gly Gln Gly Gly Gly Gly Gly Gly Gly Ser Gly Gly Ile Ala Glu Ala  
 340 345 350  
 Gly Ser Gly His Met Asn Tyr Ile Gln Val Thr Pro Gln Glu Lys Glu  
 355 360 365  
 Ala Ile Glu Arg Leu Lys Ala Leu Gly Phe Pro Glu Gly Leu Val Ile  
 370 375 380  
 Gln Ala Tyr Phe Ala Cys Glu Lys Asn Glu Asn Leu Ala Ala Asn Phe  
 385 390 395 400  
 Leu Leu Gln Gln Asn Phe Asp Glu Asp  
 405

<210> 171  
 <211> 614  
 <212> PRT  
 <213> Homo sapiens

<400> 171

Met Ser Gly Ile Lys Lys Gln Lys Thr Glu Asn Gln Gln Lys Ser Thr  
 1 5 10 15  
 Asn Val Val Tyr Gln Ala His His Val Ser Arg Asn Lys Arg Gly Gln  
 20 25 30  
 Val Val Gly Thr Arg Gly Gly Phe Arg Gly Cys Thr Val Trp Leu Thr  
 35 40 45

Gly Leu Ser Gly Ala Gly Lys Thr Thr Ile Ser Phe Ala Leu Glu Glu  
 50 55 60  
 Tyr Leu Val Ser His Ala Ile Pro Cys Tyr Ser Leu Asp Gly Asp Asn  
 65 70 75 80  
 Val Arg His Gly Leu Asn Arg Asn Leu Gly Phe Ser Pro Gly Asp Arg  
 85 90 95  
 Glu Glu Asn Ile Arg Arg Ile Ala Glu Val Ala Lys Leu Phe Ala Asp  
 100 105 110  
 Ala Gly Leu Val Cys Ile Thr Ser Phe Ile Ser Pro Phe Ala Lys Asp  
 115 120 125  
 Arg Glu Asn Ala Arg Lys Ile His Glu Ser Ala Gly Leu Pro Phe Phe  
 130 135 140  
 Glu Ile Phe Val Asp Ala Pro Leu Asn Ile Cys Glu Ser Arg Asp Val  
 145 150 155 160  
 Lys Gly Leu Tyr Lys Lys Ala Arg Ala Gly Glu Ile Lys Gly Phe Thr  
 165 170 175  
 Gly Ile Asp Ser Asp Tyr Glu Lys Pro Glu Thr Pro Glu Arg Val Leu  
 180 185 190  
 Lys Thr Asn Leu Ser Thr Val Ser Asp Cys Val His Gln Val Val Glu  
 195 200 205  
 Leu Leu Gln Glu Gln Asn Ile Val Pro Tyr Thr Ile Ile Lys Asp Ile  
 210 215 220  
 His Glu Leu Phe Val Pro Glu Asn Lys Leu Asp His Val Arg Ala Glu  
 225 230 235 240  
 Ala Glu Thr Leu Pro Ser Leu Ser Ile Thr Lys Leu Asp Leu Gln Trp  
 245 250 255  
 Val Gln Val Leu Ser Glu Gly Trp Ala Thr Pro Leu Lys Gly Phe Met  
 260 265 270  
 Arg Glu Lys Glu Tyr Leu Gln Val Met His Phe Asp Thr Leu Leu Asp  
 275 280 285  
 Asp Gly Val Ile Asn Met Ser Ile Pro Ile Val Leu Pro Val Ser Ala  
 290 295 300  
 Glu Asp Lys Thr Arg Leu Glu Gly Cys Ser Lys Phe Val Leu Ala His  
 305 310 315 320  
 Gly Gly Arg Arg Val Ala Ile Leu Arg Asp Ala Glu Phe Tyr Glu His  
 325 330 335  
 Arg Lys Glu Glu Arg Cys Ser Arg Val Trp Gly Thr Thr Cys Thr Lys  
 340 345 350  
 His Pro His Ile Lys Met Val Met Glu Ser Gly Asp Trp Leu Val Gly  
 355 360 365

Gly Asp Leu Gln Val Leu Glu Lys Ile Arg Trp Asn Asp Gly Leu Asp  
370 375 380

Gln Tyr Arg Leu Thr Pro Leu Glu Leu Lys Gln Lys Cys Lys Glu Met  
385 390 395 400

Asn Ala Asp Ala Val Phe Ala Phe Gln Leu Arg Asn Pro Val His Asn  
405 410 415

Gly His Ala Leu Leu Met Gln Asp Thr Arg Arg Arg Leu Leu Glu Arg  
420 425 430

Gly Tyr Lys His Pro Val Leu Leu Leu His Pro Leu Gly Gly Trp Thr  
435 440 445

Lys Asp Asp Asp Val Pro Leu Asp Trp Arg Met Lys Gln His Ala Ala  
450 455 460

Val Leu Glu Glu Gly Val Leu Asp Pro Lys Ser Thr Ile Val Ala Ile  
465 470 475 480

Phe Pro Ser Pro Met Leu Tyr Ala Gly Pro Thr Glu Val Gln Trp His  
485 490 495

Cys Arg Ser Arg Met Ile Ala Gly Ala Asn Phe Tyr Ile Val Gly Arg  
500 505 510

Asp Pro Ala Gly Met Pro His Pro Glu Thr Lys Lys Asp Leu Tyr Glu  
515 520 525

Pro Thr His Gly Gly Lys Val Leu Ser Met Ala Pro Gly Leu Thr Ser  
530 535 540

Val Glu Ile Ile Pro Phe Arg Val Ala Ala Tyr Asn Lys Ala Lys Lys  
545 550 555 560

Ala Met Asp Phe Tyr Asp Leu Ala Arg His Asn Glu Phe Asp Phe Ile  
565 570 575

Ser Gly Thr Arg Met Arg Lys Leu Ala Arg Glu Gly Glu Asn Pro Pro  
580 585 590

Asp Gly Phe Met Ala Pro Lys Ala Trp Lys Val Leu Thr Asp Tyr Tyr  
595 600 605

Arg Ser Leu Glu Lys Asn  
610

<210> 172  
<211> 798  
<212> PRT  
<213> Homo sapiens

<400> 172

Met Asn Leu Gln Pro Ile Phe Trp Ile Gly Leu Ile Ser Ser Val Cys  
1 5 10 15

Cys Val Phe Ala Gln Thr Asp Glu Asn Arg Cys Leu Lys Ala Asn Ala  
20 25 30

Lys Ser Cys Gly Glu Cys Ile Gln Ala Gly Pro Asn Cys Gly Trp Cys  
 35 40 45  
 Thr Asn Ser Thr Phe Leu Gln Glu Gly Met Pro Thr Ser Ala Arg Cys  
 50 55 60  
 Asp Asp Leu Glu Ala Leu Lys Lys Lys Gly Cys Pro Pro Asp Asp Ile  
 65 70 75 80  
 Glu Asn Pro Arg Gly Ser Lys Asp Ile Lys Lys Asn Lys Asn Val Thr  
 85 90 95  
 Asn Arg Ser Lys Gly Thr Ala Glu Lys Leu Lys Pro Glu Asp Ile His  
 100 105 110  
 Gln Ile Gln Pro Gln Gln Leu Val Leu Arg Leu Arg Ser Gly Glu Pro  
 115 120 125  
 Gln Thr Phe Thr Leu Lys Phe Lys Arg Ala Glu Asp Tyr Pro Ile Asp  
 130 135 140  
 Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Glu  
 145 150 155 160  
 Asn Val Lys Ser Leu Gly Thr Asp Leu Met Asn Glu Met Arg Arg Ile  
 165 170 175  
 Thr Ser Asp Phe Arg Ile Gly Phe Gly Ser Phe Val Glu Lys Thr Val  
 180 185 190  
 Met Pro Tyr Ile Ser Thr Thr Pro Ala Lys Leu Arg Asn Pro Cys Thr  
 195 200 205  
 Ser Glu Gln Asn Cys Thr Thr Pro Phe Ser Tyr Lys Asn Val Leu Ser  
 210 215 220  
 Leu Thr Asn Lys Gly Glu Val Phe Asn Glu Leu Val Gly Lys Gln Arg  
 225 230 235 240  
 Ile Ser Gly Asn Leu Asp Ser Pro Glu Gly Gly Phe Asp Ala Ile Met  
 245 250 255  
 Gln Val Ala Val Cys Gly Ser Leu Ile Gly Trp Arg Asn Val Thr Arg  
 260 265 270  
 Leu Leu Val Phe Ser Thr Asp Ala Gly Phe His Phe Ala Gly Asp Gly  
 275 280 285  
 Lys Leu Gly Gly Ile Val Leu Pro Asn Asp Gly Gln Cys His Leu Glu  
 290 295 300  
 Asn Asn Met Tyr Thr Met Ser His Tyr Tyr Asp Tyr Pro Ser Ile Ala  
 305 310 315 320  
 His Leu Val Gln Lys Leu Ser Glu Asn Asn Ile Gln Thr Ile Phe Ala  
 325 330 335  
 Val Thr Glu Glu Phe Gln Pro Val Tyr Lys Glu Leu Lys Asn Leu Ile

340	345	350
Pro Lys Ser Ala Val Gly Thr 355	Leu Ser Ala Asn Ser 360	Ser Asn Val Ile 365
Gln Leu Ile Ile Asp Ala Tyr 370	Asn Ser Leu Ser 375	Ser Glu Val Ile Leu 380
Glu Asn Gly Lys Leu Ser 385	Glu Gly Val Thr 390	Ile Ser Tyr Lys Ser Tyr 395 400
Cys Lys Asn Gly Val Asn Gly Thr 405	Gly Glu Asn Gly Arg 410	Lys Cys Ser 415
Asn Ile Ser Ile Gly Asp Glu Val 420	Gln Phe Glu Ile Ser 425	Ile Thr Ser 430
Asn Lys Cys Pro Lys Lys Asp 435	Ser Asp Ser Phe Lys 440	Ile Arg Pro Leu 445
Gly Phe Thr Glu Glu Val 450	Glu Val Ile Leu Gln Tyr 455	Ile Cys Glu Cys 460
Glu Cys Gln Ser Glu Gly Ile Pro 465	Glu Ser Pro Lys Cys His 470 475	Glu Gly 480
Asn Gly Thr Phe Glu Cys Gly Ala Cys 485	Arg Cys Asn Glu Gly Arg 490	Val 495
Gly Arg His Cys Glu Cys Ser Thr 500	Asp Glu Val Asn Ser 505	Glu Asp Met 510
Asp Ala Tyr Cys Arg Lys Glu Asn Ser 515	Ser Ser Glu Ile Cys Ser Asn Asn 520 525	
Gly Glu Cys Val Cys Gly Gln Cys Val 530	Cys Arg Lys Arg Asp Asn Thr 535 540	
Asn Glu Ile Tyr Ser Gly Lys Phe Cys 545	Glu Cys Asp Asn Phe Asn Cys 550 555	
Asp Arg Ser Asn Gly Leu Ile Cys Gly 565	Gly Asn Gly Val Cys Lys Cys 570 575	
Arg Val Cys Glu Cys Asn Pro Asn Tyr Thr 580	Gly Ser Ala Cys Asp Cys 585 590	
Ser Leu Asp Thr Ser Thr Cys Glu Ala Ser 595	Asn Gly Gln Ile Cys Asn 600 605	
Gly Arg Gly Ile Cys Glu Cys Gly Val 610	Cys Lys Cys Thr Asp Pro Lys 615 620	
Phe Gln Gly Gln Thr Cys Glu Met Cys 625	Gln Thr Cys Leu Gly Val Cys 630 635	
Ala Glu His Lys Glu Cys Val Gln Cys Arg 645	Ala Phe Asn Lys Gly Glu 650 655	



Lys Lys Asp Thr Cys Thr Gln Glu Cys Ser Tyr Phe Asn Ile Thr Lys  
660 665 670

Val Glu Ser Arg Asp Lys Leu Pro Gln Pro Val Gln Pro Asp Pro Val  
675 680 685

Ser His Cys Lys Glu Lys Asp Val Asp Asp Cys Trp Phe Tyr Phe Thr  
690 695 700

Tyr Ser Val Asn Gly Asn Asn Glu Val Met Val His Val Val Glu Asn  
705 710 715 720

Pro Glu Cys Pro Thr Gly Pro Asp Ile Ile Pro Ile Val Ala Gly Val  
725 730 735

Val Ala Gly Ile Val Leu Ile Gly Leu Ala Leu Leu Leu Ile Trp Lys  
740 745 750

Leu Leu Met Ile Ile His Asp Arg Arg Glu Phe Ala Lys Phe Glu Lys  
755 760 765

Glu Lys Met Asn Ala Lys Trp Asp Thr Gly Glu Asn Pro Ile Tyr Lys  
770 775 780

Ser Ala Val Thr Thr Val Val Asn Pro Lys Tyr Glu Gly Lys  
785 790 795

<210> 173  
<211> 502  
<212> PRT  
<213> Homo sapiens

<400> 173

Met Ala Ser Lys Lys Leu Gly Ala Asp Phe His Gly Thr Phe Ser Tyr  
1 5 10 15

Leu Asp Asp Val Pro Phe Lys Thr Gly Asp Lys Phe Lys Thr Pro Ala  
20 25 30

Lys Val Gly Leu Pro Ile Gly Phe Ser Leu Pro Asp Cys Leu Gln Val  
35 40 45

Val Arg Glu Val Gln Tyr Asp Phe Ser Leu Glu Lys Lys Thr Ile Glu  
50 55 60

Trp Ala Glu Glu Ile Lys Lys Ile Glu Glu Ala Glu Arg Glu Ala Glu  
65 70 75 80

Cys Lys Ile Ala Glu Ala Glu Ala Lys Val Asn Ser Lys Ser Gly Pro  
85 90 95

Glu Gly Asp Ser Lys Met Ser Phe Ser Lys Thr His Ser Thr Ala Thr  
100 105 110

Met Pro Pro Pro Ile Asn Pro Ile Leu Ala Ser Leu Gln His Asn Ser  
115 120 125

Ile Leu Thr Pro Thr Arg Val Ser Ser Ser Ala Thr Lys Gln Lys Val  
130 135 140

Leu Ser Pro Pro His Ile Lys Ala Asp Phe Asn Leu Ala Asp Phe Glu  
145 150 155 160

Cys Glu Glu Asp Pro Phe Asp Asn Leu Glu Leu Lys Thr Ile Asp Glu  
165 170 175

Lys Glu Glu Leu Arg Asn Ile Leu Val Gly Thr Thr Gly Pro Ile Met  
180 185 190

Ala Gln Leu Leu Asp Asn Asn Leu Pro Arg Gly Gly Ser Gly Ser Val  
195 200 205

Leu Gln Asp Glu Glu Val Leu Ala Ser Leu Glu Arg Ala Thr Leu Asp  
210 215 220

Phe Lys Pro Leu His Lys Pro Asn Gly Phe Ile Thr Leu Pro Gln Leu  
225 230 235 240

Gly Asn Cys Glu Lys Met Ser Leu Ser Ser Lys Val Ser Leu Pro Pro  
245 250 255

Ile Pro Ala Val Ser Asn Ile Lys Ser Leu Ser Phe Pro Lys Leu Asp  
260 265 270

Ser Asp Asp Ser Asn Gln Lys Thr Ala Lys Leu Ala Ser Thr Phe His  
275 280 285

Ser Thr Ser Cys Leu Arg Asn Gly Thr Phe Gln Asn Ser Leu Lys Pro  
290 295 300

Ser Thr Gln Ser Ser Ala Ser Glu Leu Asn Gly His His Thr Leu Gly  
305 310 315 320

Leu Ser Ala Leu Asn Leu Asp Ser Gly Thr Glu Met Pro Ala Leu Thr  
325 330 335

Ser Ser Gln Met Pro Ser Leu Ser Val Leu Ser Val Cys Thr Glu Glu  
340 345 350

Ser Ser Pro Pro Asn Thr Gly Pro Thr Val Thr Pro Pro Asn Phe Ser  
355 360 365

Val Ser Gln Val Pro Asn Met Pro Ser Cys Pro Gln Ala Tyr Ser Glu  
370 375 380

Leu Gln Met Leu Ser Pro Ser Glu Arg Gln Cys Val Glu Thr Val Val  
385 390 395 400

Asn Met Gly Tyr Ser Tyr Glu Cys Val Leu Arg Ala Met Lys Lys Lys  
405 410 415

Gly Glu Asn Ile Glu Gln Ile Leu Asp Tyr Leu Phe Ala His Gly Gln  
420 425 430

Leu Cys Glu Lys Gly Phe Asp Pro Leu Leu Val Glu Glu Ala Leu Glu  
435 440 445

Met His Gln Cys Ser Glu Glu Lys Met Met Glu Phe Leu Gln Leu Met  
450 455 460

Ser Lys Phe Lys Glu Met Gly Phe Glu Leu Lys Asp Ile Lys Glu Val  
465 470 475 480

Leu Leu Leu His Asn Asn Asp Gln Asp Asn Ala Leu Glu Asp Leu Met  
485 490 495

Ala Arg Ala Gly Ala Ser  
500

<210> 174  
<211> 545  
<212> PRT  
<213> Homo sapiens

<400> 174

Met Ser Asn Asn Gly Leu Asp Ile Gln Asp Lys Pro Pro Ala Pro Pro  
1 5 10 15

Met Arg Asn Thr Ser Thr Met Ile Gly Val Gly Ser Lys Asp Ala Gly  
20 25 30

Thr Leu Asn His Gly Ser Lys Pro Leu Pro Pro Asn Pro Glu Glu Lys  
35 40 45

Lys Lys Lys Asp Arg Phe Tyr Arg Ser Ile Leu Pro Gly Asp Lys Thr  
50 55 60

Asn Lys Lys Lys Glu Lys Glu Arg Pro Glu Ile Ser Leu Pro Ser Asp  
65 70 75 80

Phe Glu His Thr Ile His Val Gly Phe Asp Ala Val Thr Gly Glu Phe  
85 90 95

Thr Gly Met Pro Glu Gln Trp Ala Arg Leu Leu Gln Thr Ser Asn Ile  
100 105 110

Thr Lys Ser Glu Gln Lys Lys Asn Pro Gln Ala Val Leu Asp Val Leu  
115 120 125

Glu Phe Tyr Asn Ser Lys Lys Thr Ser Asn Ser Gln Lys Tyr Met Ser  
130 135 140

Phe Thr Asp Lys Ser Ala Glu Asp Tyr Asn Ser Ser Asn Ala Leu Asn  
145 150 155 160

Val Lys Ala Val Ser Glu Thr Pro Ala Val Pro Pro Val Ser Glu Asp  
165 170 175

Glu Asp Asp Asp Asp Asp Ala Thr Pro Pro Pro Val Ile Ala Pro  
180 185 190

Arg Pro Glu His Thr Lys Ser Val Tyr Thr Arg Ser Val Ile Glu Pro  
195 200 205

Leu Pro Val Thr Pro Thr Arg Asp Val Ala Thr Ser Pro Ile Ser Pro  
210 215 220

Thr Glu Asn Asn Thr Thr Pro Pro Asp Ala Leu Thr Arg Asn Thr Glu  
225 230 235 240

Lys Gln Lys Lys Lys Pro Lys Met Ser Asp Glu Glu Ile Leu Glu Lys  
 245 250 255  
 Leu Arg Ser Ile Val Ser Val Gly Asp Pro Lys Lys Lys Tyr Thr Arg  
 260 265 270  
 Phe Glu Lys Ile Gly Gln Gly Ala Ser Gly Thr Val Tyr Thr Ala Met  
 275 280 285  
 Asp Val Ala Thr Gly Gln Glu Val Ala Ile Lys Gln Met Asn Leu Gln  
 290 295 300  
 Gln Gln Pro Lys Lys Glu Leu Ile Ile Asn Glu Ile Leu Val Met Arg  
 305 310 315 320  
 Glu Asn Lys Asn Pro Asn Ile Val Asn Tyr Leu Asp Ser Tyr Leu Val  
 325 330 335  
 Gly Asp Glu Leu Trp Val Val Met Glu Tyr Leu Ala Gly Gly Ser Leu  
 340 345 350  
 Thr Asp Val Val Thr Glu Thr Cys Met Asp Glu Gly Gln Ile Ala Ala  
 355 360 365  
 Val Cys Arg Glu Cys Leu Gln Ala Leu Glu Phe Leu His Ser Asn Gln  
 370 375 380  
 Val Ile His Arg Asp Ile Lys Ser Asp Asn Ile Leu Leu Gly Met Asp  
 385 390 395 400  
 Gly Ser Val Lys Leu Thr Asp Phe Gly Phe Cys Ala Gln Ile Thr Pro  
 405 410 415  
 Glu Gln Ser Lys Arg Ser Thr Met Val Gly Thr Pro Tyr Trp Met Ala  
 420 425 430  
 Pro Glu Val Val Thr Arg Lys Ala Tyr Gly Pro Lys Val Asp Ile Trp  
 435 440 445  
 Ser Leu Gly Ile Met Ala Ile Glu Met Ile Glu Gly Glu Pro Pro Tyr  
 450 455 460  
 Leu Asn Glu Asn Pro Leu Arg Ala Leu Tyr Leu Ile Ala Thr Asn Gly  
 465 470 475 480  
 Thr Pro Glu Leu Gln Asn Pro Glu Lys Leu Ser Ala Ile Phe Arg Asp  
 485 490 495  
 Phe Leu Asn Arg Cys Leu Asp Met Asp Val Glu Lys Arg Gly Ser Ala  
 500 505 510  
 Lys Glu Leu Leu Gln His Gln Phe Leu Lys Ile Ala Lys Pro Leu Ser  
 515 520 525  
 Ser Leu Thr Pro Leu Ile Ala Ala Lys Glu Ala Thr Lys Asn Asn  
 530 535 540  
 His  
 545

<210> 175  
 <211> 1360  
 <212> PRT  
 <213> Homo sapiens

<400> 175

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Met Ser Arg Gln Ser Thr Leu Tyr Ser Phe Phe Pro Lys Ser Pro Ala
1          5          10          15

Leu Ser Asp Ala Asn Lys Ala Ser Ala Arg Ala Ser Arg Glu Gly Gly
20          25          30

Arg Ala Ala Ala Ala Pro Gly Ala Ser Pro Ser Pro Gly Gly Asp Ala
35          40          45

Ala Trp Ser Glu Ala Gly Pro Gly Pro Arg Pro Leu Ala Arg Ser Ala
50          55          60

Ser Pro Pro Lys Ala Lys Asn Leu Asn Gly Gly Leu Arg Arg Ser Val
65          70          75          80

Ala Pro Ala Ala Pro Thr Ser Cys Asp Phe Ser Pro Gly Asp Leu Val
85          90          95

Trp Ala Lys Met Glu Gly Tyr Pro Trp Trp Pro Cys Leu Val Tyr Asn
100         105         110

His Pro Phe Asp Gly Thr Phe Ile Arg Glu Lys Gly Lys Ser Val Arg
115         120         125

Val His Val Gln Phe Phe Asp Asp Ser Pro Thr Arg Gly Trp Val Ser
130         135         140

Lys Arg Leu Leu Lys Pro Tyr Thr Gly Ser Lys Ser Lys Glu Ala Gln
145         150         155         160

Lys Gly Gly His Phe Tyr Ser Ala Lys Pro Glu Ile Leu Arg Ala Met
165         170         175

Gln Arg Ala Asp Glu Ala Leu Asn Lys Asp Lys Ile Lys Arg Leu Glu
180         185         190

Leu Ala Val Cys Asp Glu Pro Ser Glu Pro Glu Glu Glu Glu Glu Met
195         200         205

Glu Val Gly Thr Thr Tyr Val Thr Asp Lys Ser Glu Glu Asp Asn Glu
210         215         220

Ile Glu Ser Glu Glu Glu Val Gln Pro Lys Thr Gln Gly Ser Arg Arg
225         230         235         240

Ser Ser Arg Gln Ile Lys Lys Arg Arg Val Ile Ser Asp Ser Glu Ser
245         250         255

Asp Ile Gly Gly Ser Asp Val Glu Phe Lys Pro Asp Thr Lys Glu Glu
260         265         270

Gly Ser Ser Asp Glu Ile Ser Ser Gly Val Gly Asp Ser Glu Ser Glu
275         280         285

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Gly Leu Asn Ser Pro Val Lys Val Ala Arg Lys Arg Lys Arg Met Val  
 290 295 300  
 Thr Gly Asn Gly Ser Leu Lys Arg Lys Ser Ser Arg Lys Glu Thr Pro  
 305 310 315 320  
 Ser Ala Thr Lys Gln Ala Thr Ser Ile Ser Ser Glu Thr Lys Asn Thr  
 325 330 335  
 Leu Arg Ala Phe Ser Ala Pro Gln Asn Ser Glu Ser Gln Ala His Val  
 340 345 350  
 Ser Gly Gly Gly Asp Asp Ser Ser Arg Pro Thr Val Trp Tyr His Glu  
 355 360 365  
 Thr Leu Glu Trp Leu Lys Glu Glu Lys Arg Arg Asp Glu His Arg Arg  
 370 375 380  
 Arg Pro Asp His Pro Asp Phe Asp Ala Ser Thr Leu Tyr Val Pro Glu  
 385 390 395 400  
 Asp Phe Leu Asn Ser Cys Thr Pro Gly Met Arg Lys Trp Trp Gln Ile  
 405 410 415  
 Lys Ser Gln Asn Phe Asp Leu Val Ile Cys Tyr Lys Val Gly Lys Phe  
 420 425 430  
 Tyr Glu Leu Tyr His Met Asp Ala Leu Ile Gly Val Ser Glu Leu Gly  
 435 440 445  
 Leu Val Phe Met Lys Gly Asn Trp Ala His Ser Gly Phe Pro Glu Ile  
 450 455 460  
 Ala Phe Gly Arg Tyr Ser Asp Ser Leu Val Gln Lys Gly Tyr Lys Val  
 465 470 475 480  
 Ala Arg Val Glu Gln Thr Glu Thr Pro Glu Met Met Glu Ala Arg Cys  
 485 490 495  
 Arg Lys Met Ala His Ile Ser Lys Tyr Asp Arg Val Val Arg Arg Glu  
 500 505 510  
 Ile Cys Arg Ile Ile Thr Lys Gly Thr Gln Thr Tyr Ser Val Leu Glu  
 515 520 525  
 Gly Asp Pro Ser Glu Asn Tyr Ser Lys Tyr Leu Leu Ser Leu Lys Glu  
 530 535 540  
 Lys Glu Glu Asp Ser Ser Gly His Thr Arg Ala Tyr Gly Val Cys Phe  
 545 550 555 560  
 Val Asp Thr Ser Leu Gly Lys Phe Phe Ile Gly Gln Phe Ser Asp Asp  
 565 570 575  
 Arg His Cys Ser Arg Phe Arg Thr Leu Val Ala His Tyr Pro Pro Val  
 580 585 590  
 Gln Val Leu Phe Glu Lys Gly Asn Leu Ser Lys Glu Thr Lys Thr Ile

595	600	605
Leu Lys Ser Ser Leu Ser Cys Ser Leu Gln Glu Gly Leu Ile Pro Gly 610 615 620		
Ser Gln Phe Trp Asp Ala Ser Lys Thr Leu Arg Thr Leu Leu Glu Glu 625 630 635 640		
Glu Tyr Phe Arg Glu Lys Leu Ser Asp Gly Ile Gly Val Met Leu Pro 645 650 655		
Gln Val Leu Lys Gly Met Thr Ser Glu Ser Asp Ser Ile Gly Leu Thr 660 665 670		
Pro Gly Glu Lys Ser Glu Leu Ala Leu Ser Ala Leu Gly Gly Cys Val 675 680 685		
Phe Tyr Leu Lys Lys Cys Leu Ile Asp Gln Glu Leu Leu Ser Met Ala 690 695 700		
Asn Phe Glu Glu Tyr Ile Pro Leu Asp Ser Asp Thr Val Ser Thr Thr 705 710 715 720		
Arg Ser Gly Ala Ile Phe Thr Lys Ala Tyr Gln Arg Met Val Leu Asp 725 730 735		
Ala Val Thr Leu Asn Asn Leu Glu Ile Phe Leu Asn Gly Thr Asn Gly 740 745 750		
Ser Thr Glu Gly Thr Leu Leu Glu Arg Val Asp Thr Cys His Thr Pro 755 760 765		
Phe Gly Lys Arg Leu Leu Lys Gln Trp Leu Cys Ala Pro Leu Cys Asn 770 775 780		
His Tyr Ala Ile Asn Asp Arg Leu Asp Ala Ile Glu Asp Leu Met Val 785 790 795 800		
Val Pro Asp Lys Ile Ser Glu Val Val Glu Leu Leu Lys Lys Leu Pro 805 810 815		
Asp Leu Glu Arg Leu Leu Ser Lys Ile His Asn Val Gly Ser Pro Leu 820 825 830		
Lys Ser Gln Asn His Pro Asp Ser Arg Ala Ile Met Tyr Glu Glu Thr 835 840 845		
Thr Tyr Ser Lys Lys Lys Ile Ile Asp Phe Leu Ser Ala Leu Glu Gly 850 855 860		
Phe Lys Val Met Cys Lys Ile Ile Gly Ile Met Glu Glu Val Ala Asp 865 870 875 880		
Gly Phe Lys Ser Lys Ile Leu Lys Gln Val Ile Ser Leu Gln Thr Lys 885 890 895		
Asn Pro Glu Gly Arg Phe Pro Asp Leu Thr Val Glu Leu Asn Arg Trp 900 905 910		

Asp Thr Ala Phe Asp His Glu Lys Ala Arg Lys Thr Gly Leu Ile Thr  
 915 920 925  
 Pro Lys Ala Gly Phe Asp Ser Asp Tyr Asp Gln Ala Leu Ala Asp Ile  
 930 935 940  
 Arg Glu Asn Glu Gln Ser Leu Leu Glu Tyr Leu Glu Lys Gln Arg Asn  
 945 950 955 960  
 Arg Ile Gly Cys Arg Thr Ile Val Tyr Trp Gly Ile Gly Arg Asn Arg  
 965 970 975  
 Tyr Gln Leu Glu Ile Pro Glu Asn Phe Thr Thr Arg Asn Leu Pro Glu  
 980 985 990  
 Glu Tyr Glu Leu Lys Ser Thr Lys Lys Gly Cys Lys Arg Tyr Trp Thr  
 995 1000 1005  
 Lys Thr Ile Glu Lys Lys Leu Ala Asn Leu Ile Asn Ala Glu Glu  
 1010 1015 1020  
 Arg Arg Asp Val Ser Leu Lys Asp Cys Met Arg Arg Leu Phe Tyr  
 1025 1030 1035  
 Asn Phe Asp Lys Asn Tyr Lys Asp Trp Gln Ser Ala Val Glu Cys  
 1040 1045 1050  
 Ile Ala Val Leu Asp Val Leu Leu Cys Leu Ala Asn Tyr Ser Arg  
 1055 1060 1065  
 Gly Gly Asp Gly Pro Met Cys Arg Pro Val Ile Leu Leu Pro Glu  
 1070 1075 1080  
 Asp Thr Pro Pro Phe Leu Glu Leu Lys Gly Ser Arg His Pro Cys  
 1085 1090 1095  
 Ile Thr Lys Thr Phe Phe Gly Asp Asp Phe Ile Pro Asn Asp Ile  
 1100 1105 1110  
 Leu Ile Gly Cys Glu Glu Glu Glu Gln Glu Asn Gly Lys Ala Tyr  
 1115 1120 1125  
 Cys Val Leu Val Thr Gly Pro Asn Met Gly Gly Lys Ser Thr Leu  
 1130 1135 1140  
 Met Arg Gln Ala Gly Leu Leu Ala Val Met Ala Gln Met Gly Cys  
 1145 1150 1155  
 Tyr Val Pro Ala Glu Val Cys Arg Leu Thr Pro Ile Asp Arg Val  
 1160 1165 1170  
 Phe Thr Arg Leu Gly Ala Ser Asp Arg Ile Met Ser Gly Glu Ser  
 1175 1180 1185  
 Thr Phe Phe Val Glu Leu Ser Glu Thr Ala Ser Ile Leu Met His  
 1190 1195 1200  
 Ala Thr Ala His Ser Leu Val Leu Val Asp Glu Leu Gly Arg Gly  
 1205 1210 1215



Thr Ala Thr Phe Asp Gly Thr Ala Ile Ala Asn Ala Val Val Lys  
 1220 1225 1230  
 Glu Leu Ala Glu Thr Ile Lys Cys Arg Thr Leu Phe Ser Thr His  
 1235 1240 1245  
 Tyr His Ser Leu Val Glu Asp Tyr Ser Gln Asn Val Ala Val Arg  
 1250 1255 1260  
 Leu Gly His Met Ala Cys Met Val Glu Asn Glu Cys Glu Asp Pro  
 1265 1270 1275  
 Ser Gln Glu Thr Ile Thr Phe Leu Tyr Lys Phe Ile Lys Gly Ala  
 1280 1285 1290  
 Cys Pro Lys Ser Tyr Gly Phe Asn Ala Ala Arg Leu Ala Asn Leu  
 1295 1300 1305  
 Pro Glu Glu Val Ile Gln Lys Gly His Arg Lys Ala Arg Glu Phe  
 1310 1315 1320  
 Glu Lys Met Asn Gln Ser Leu Arg Leu Phe Arg Glu Val Cys Leu  
 1325 1330 1335  
 Ala Ser Glu Arg Ser Thr Val Asp Ala Glu Ala Val His Lys Leu  
 1340 1345 1350  
 Leu Thr Leu Ile Lys Glu Leu  
 1355 1360  
 <210> 176  
 <211> 398  
 <212> PRT  
 <213> Homo sapiens  
 <400> 176  
 Met Gln Ser Glu Arg Gly Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe  
 1 5 10 15  
 Glu Thr Ser Lys Tyr Tyr Val Thr Ile Ile Asp Ala Pro Gly His Arg  
 20 25 30  
 Asp Phe Ile Gln Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala  
 35 40 45  
 Val Leu Ile Val Ala Ala Gly Val Gly Glu Phe Glu Ala Gly Ile Ser  
 50 55 60  
 Lys Asn Gly Gln Thr Arg Glu His Ala Leu Leu Ala Tyr Thr Leu Gly  
 65 70 75 80  
 Val Lys Gln Leu Ile Val Gly Val Asn Lys Met Asp Ser Thr Glu Pro  
 85 90 95  
 Pro Tyr Ser Gln Lys Arg Tyr Glu Glu Ile Val Lys Glu Val Ser Thr  
 100 105 110  
 Tyr Ile Lys Lys Ile Gly Tyr Asn Pro Asp Thr Val Ala Phe Val Pro  
 115 120 125

Ile Ser Gly Trp Asn Gly Asp Asn Met Leu Glu Pro Ser Ala Asn Met  
 130 135 140  
 Pro Trp Phe Lys Gly Trp Lys Val Thr Arg Lys Asp Gly Asn Ala Ser  
 145 150 155 160  
 Gly Thr Thr Leu Leu Glu Ala Leu Asp Cys Ile Leu Pro Pro Thr Arg  
 165 170 175  
 Pro Thr Asp Lys Pro Leu Gly Leu Pro Leu Gln Asp Val Tyr Lys Ile  
 180 185 190  
 Gly Gly Ile Gly Thr Val Pro Val Gly Arg Val Glu Thr Gly Val Leu  
 195 200 205  
 Lys Pro Gly Met Val Val Thr Phe Gly Pro Val Asn Val Thr Thr Glu  
 210 215 220  
 Val Lys Ser Val Glu Met His His Glu Ala Leu Gly Glu Ala Leu Pro  
 225 230 235 240  
 Gly Asp Asn Val Gly Phe Asn Val Lys Asn Val Ser Val Lys Asp Val  
 245 250 255  
 Arg Arg Gly Asn Val Ala Gly Asp Ser Lys Asn Asp Pro Pro Met Glu  
 260 265 270  
 Ala Ala Gly Phe Pro Ala Gln Val Ile Ile Leu Asn His Pro Gly Gln  
 275 280 285  
 Ile Ser Ala Gly Tyr Ala Pro Val Leu Asp Cys His Thr Ala His Ile  
 290 295 300  
 Ala Cys Lys Phe Ala Glu Leu Lys Glu Lys Ile Asp Arg Arg Ser Gly  
 305 310 315 320  
 Lys Lys Leu Glu Asp Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala  
 325 330 335  
 Ile Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser  
 340 345 350  
 Asp Tyr Pro Pro Leu Gly Cys Phe Ala Val Arg Asp Met Arg Gln Thr  
 355 360 365  
 Val Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Ala Gly Ala  
 370 375 380  
 Gly Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys  
 385 390 395  
 <210> 177  
 <211> 334  
 <212> PRT  
 <213> Homo sapiens  
 <400> 177  
 Met Ala Thr Leu Lys Glu Lys Leu Ile Ala Pro Val Ala Glu Glu Glu  
 1 5 10 15

Ala Thr Val Pro Asn Asn Lys Ile Thr Val Val Gly Val Gly Gln Val  
 20 25 30  
 Gly Met Ala Cys Ala Ile Ser Ile Leu Gly Lys Ser Leu Ala Asp Glu  
 35 40 45  
 Leu Ala Leu Val Asp Val Leu Glu Asp Lys Leu Lys Gly Glu Met Met  
 50 55 60  
 Asp Leu Gln His Gly Ser Leu Phe Leu Gln Thr Pro Lys Ile Val Ala  
 65 70 75 80  
 Asp Lys Asp Tyr Ser Val Thr Ala Asn Ser Lys Ile Val Val Val Thr  
 85 90 95  
 Ala Gly Val Arg Gln Gln Glu Gly Glu Ser Arg Leu Asn Leu Val Gln  
 100 105 110  
 Arg Asn Val Asn Val Phe Lys Phe Ile Ile Pro Gln Ile Val Lys Tyr  
 115 120 125  
 Ser Pro Asp Cys Ile Ile Ile Val Val Ser Asn Pro Val Asp Ile Leu  
 130 135 140  
 Thr Tyr Val Thr Trp Lys Leu Ser Gly Leu Pro Lys His Arg Val Ile  
 145 150 155 160  
 Gly Ser Gly Cys Asn Leu Asp Ser Ala Arg Phe Arg Tyr Leu Met Ala  
 165 170 175  
 Glu Lys Leu Gly Ile His Pro Ser Ser Cys His Gly Trp Ile Leu Gly  
 180 185 190  
 Glu His Gly Asp Ser Ser Val Ala Val Trp Ser Gly Val Asn Val Ala  
 195 200 205  
 Gly Val Ser Leu Gln Glu Leu Asn Pro Glu Met Gly Thr Asp Asn Asp  
 210 215 220  
 Ser Glu Asn Trp Lys Glu Val His Lys Met Val Val Glu Ser Ala Tyr  
 225 230 235 240  
 Glu Val Ile Lys Leu Lys Gly Tyr Thr Asn Trp Ala Ile Gly Leu Ser  
 245 250 255  
 Val Ala Asp Leu Ile Glu Ser Met Leu Lys Asn Leu Ser Arg Ile His  
 260 265 270  
 Pro Val Ser Thr Met Val Lys Gly Met Tyr Gly Ile Glu Asn Glu Val  
 275 280 285  
 Phe Leu Ser Leu Pro Cys Ile Leu Asn Ala Arg Gly Leu Thr Ser Val  
 290 295 300  
 Ile Asn Gln Lys Leu Lys Asp Asp Glu Val Ala Gln Leu Lys Lys Ser  
 305 310 315 320  
 Ala Asp Thr Leu Trp Asp Ile Gln Lys Asp Leu Lys Asp Leu  
 325 330

<210> 178  
 <211> 364  
 <212> PRT  
 <213> Homo sapiens

<400> 178

Met Tyr Leu Ser Arg Phe Leu Ser Ile His Ala Leu Trp Val Thr Val  
 1 5 10 15

Ser Ser Val Met Gln Pro Tyr Pro Leu Val Trp Gly His Tyr Asp Leu  
 20 25 30

Cys Lys Thr Gln Ile Tyr Thr Glu Glu Gly Lys Val Trp Asp Tyr Met  
 35 40 45

Ala Cys Gln Pro Glu Ser Thr Asp Met Thr Lys Tyr Leu Lys Val Lys  
 50 55 60

Leu Asp Pro Pro Asp Ile Thr Cys Gly Asp Pro Pro Glu Thr Phe Cys  
 65 70 75 80

Ala Met Gly Asn Pro Tyr Met Cys Asn Asn Glu Cys Asp Ala Ser Thr  
 85 90 95

Pro Glu Leu Ala His Pro Pro Glu Leu Met Phe Asp Phe Glu Gly Arg  
 100 105 110

His Pro Ser Thr Phe Trp Gln Ser Ala Thr Trp Lys Glu Tyr Pro Lys  
 115 120 125

Pro Leu Gln Val Asn Ile Thr Leu Ser Trp Ser Lys Thr Ile Glu Leu  
 130 135 140

Thr Asp Asn Ile Val Ile Thr Phe Glu Ser Gly Arg Pro Asp Gln Met  
 145 150 155 160

Ile Leu Glu Lys Ser Leu Asp Tyr Gly Arg Thr Trp Gln Pro Tyr Gln  
 165 170 175

Tyr Tyr Ala Thr Asp Cys Leu Asp Ala Phe His Met Asp Pro Lys Ser  
 180 185 190

Val Lys Asp Leu Ser Gln His Thr Val Leu Glu Ile Ile Cys Thr Glu  
 195 200 205

Glu Tyr Ser Thr Gly Tyr Thr Thr Asn Ser Lys Ile Ile His Phe Glu  
 210 215 220

Ile Lys Asp Arg Phe Ala Phe Phe Ala Gly Pro Arg Leu Arg Asn Met  
 225 230 235 240

Ala Ser Leu Tyr Gly Gln Leu Asp Thr Thr Lys Lys Leu Arg Asp Phe  
 245 250 255

Phe Thr Val Thr Asp Leu Arg Ile Arg Leu Leu Arg Pro Ala Val Gly  
 260 265 270

Glu Ile Phe Val Asp Glu Leu His Leu Ala Arg Tyr Phe Tyr Ala Ile  
 275 280 285

Ser Asp Ile Lys Val Arg Gly Arg Cys Lys Cys Asn Leu His Ala Thr  
290 295 300

Val Cys Val Tyr Asp Asn Ser Lys Leu Thr Cys Glu Cys Glu His Asn  
305 310 315 320

Thr Thr Gly Pro Asp Cys Gly Lys Cys Lys Lys Asn Tyr Gln Gly Arg  
325 330 335

Pro Trp Ser Pro Gly Ser Tyr Leu Pro Ile Pro Lys Gly Thr Ala Asn  
340 345 350

Thr Cys Ile Pro Ser Ile Ser Ser Ile Gly Ser Lys  
355 360

<210> 179  
<211> 416  
<212> PRT  
<213> Homo sapiens

<400> 179

Met His Thr Asp Pro Asp Tyr Ser Ala Ala Tyr Val Val Ile Glu Thr  
1 5 10 15

Asp Ala Glu Asp Gly Ile Lys Gly Cys Gly Ile Thr Phe Thr Leu Gly  
20 25 30

Lys Gly Thr Glu Val Val Val Cys Ala Val Asn Ala Leu Ala His His  
35 40 45

Val Leu Asn Lys Asp Leu Lys Asp Ile Val Gly Asp Phe Arg Gly Phe  
50 55 60

Tyr Arg Gln Leu Thr Ser Asp Gly Gln Leu Arg Trp Ile Gly Pro Glu  
65 70 75 80

Lys Gly Val Val His Leu Ala Thr Ala Ala Val Leu Asn Ala Val Trp  
85 90 95

Asp Leu Trp Ala Lys Gln Glu Gly Lys Pro Val Trp Lys Leu Leu Val  
100 105 110

Asp Met Asp Pro Arg Met Leu Val Ser Cys Ile Asp Phe Arg Tyr Ile  
115 120 125

Thr Asp Val Leu Thr Glu Glu Asp Ala Leu Glu Ile Leu Gln Lys Gly  
130 135 140

Gln Ile Gly Lys Lys Glu Arg Glu Lys Gln Met Leu Ala Gln Gly Tyr  
145 150 155 160

Pro Ala Tyr Thr Thr Ser Cys Ala Trp Leu Gly Tyr Ser Asp Asp Thr  
165 170 175

Leu Lys Gln Leu Cys Ala Gln Ala Leu Lys Asp Gly Trp Thr Arg Phe  
180 185 190

Lys Val Lys Val Gly Ala Asp Leu Gln Asp Asp Met Arg Arg Cys Gln  
195 200 205

Ile Ile Arg Asp Met Ile Gly Pro Glu Lys Thr Leu Met Met Asp Ala  
210 215 220

Asn Gln Arg Trp Asp Val Pro Glu Ala Val Glu Trp Met Ser Lys Leu  
225 230 235 240

Ala Lys Phe Lys Pro Leu Trp Ile Glu Glu Pro Thr Ser Pro Asp Asp  
245 250 255

Ile Leu Gly His Ala Thr Ile Ser Lys Ala Leu Val Pro Leu Gly Ile  
260 265 270

Gly Ile Ala Thr Gly Glu Gln Cys His Asn Arg Val Ile Phe Lys Gln  
275 280 285

Leu Leu Gln Ala Lys Ala Leu Gln Phe Leu Gln Ile Asp Ser Cys Arg  
290 295 300

Leu Gly Ser Val Asn Glu Asn Leu Ser Val Leu Leu Met Ala Lys Lys  
305 310 315 320

Phe Glu Ile Pro Val Cys Pro His Ala Gly Gly Val Gly Leu Cys Glu  
325 330 335

Leu Val Gln His Leu Ile Ile Phe Asp Tyr Ile Ser Val Ser Ala Ser  
340 345 350

Leu Glu Asn Arg Val Cys Glu Tyr Val Asp His Leu His Glu His Phe  
355 360 365

Lys Tyr Pro Val Met Ile Gln Arg Ala Ser Tyr Met Pro Pro Lys Asp  
370 375 380

Pro Gly Tyr Ser Thr Glu Met Lys Glu Glu Ser Val Lys Lys His Gln  
385 390 395 400

Tyr Pro Asp Gly Glu Val Trp Lys Lys Leu Leu Pro Ala Gln Glu Asn  
405 410 415

<210> 180  
<211> 89  
<212> PRT  
<213> Homo sapiens

<400> 180

Met Ser Ser Gln Gln Gln Lys Gln Pro Cys Ile Pro Pro Pro Gln Leu  
1 5 10 15

Gln Gln Gln Gln Val Lys Gln Pro Cys Gln Pro Pro Pro Gln Glu Pro  
20 25 30

Cys Ile Pro Lys Thr Lys Glu Pro Cys His Pro Lys Val Pro Glu Pro  
35 40 45

Cys His Pro Lys Val Pro Glu Pro Cys Gln Pro Lys Leu Pro Glu Pro  
50 55 60

Cys His Pro Lys Val Pro Glu Pro Cys Pro Ser Ile Val Thr Pro Ala  
65 70 75 80

Pro Ala Gln Gln Lys Thr Lys Gln Lys  
85

<210> 181  
<211> 253  
<212> PRT  
<213> Homo sapiens

<400> 181

Met Ala Arg Ser Leu Leu Leu Pro Leu Gln Ile Leu Leu Leu Ser Leu  
1 5 10 15

Ala Leu Glu Thr Ala Gly Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp  
20 25 30

Gly Ala Pro Cys Ala Arg Gly Ser His Pro Trp Gln Val Ala Leu Leu  
35 40 45

Ser Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn Glu Arg Trp  
50 55 60

Val Leu Thr Ala Ala His Cys Lys Met Asn Glu Tyr Thr Val His Leu  
65 70 75 80

Gly Ser Asp Thr Leu Gly Asp Arg Arg Ala Gln Arg Ile Lys Ala Ser  
85 90 95

Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp  
100 105 110

Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val  
115 120 125

Lys Lys Val Arg Leu Pro Ser Arg Cys Glu Pro Pro Gly Thr Thr Cys  
130 135 140

Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro  
145 150 155 160

Ser Asp Leu Met Cys Val Asp Val Lys Leu Ile Ser Pro Gln Asp Cys  
165 170 175

Thr Lys Val Tyr Lys Asp Leu Leu Glu Asn Ser Met Leu Cys Ala Gly  
180 185 190

Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro  
195 200 205

Leu Val Cys Arg Gly Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Phe  
210 215 220

Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys  
225 230 235 240

Phe Thr Lys Trp Ile Asn Asp Thr Met Lys Lys His Arg  
245 250

<210> 182  
<211> 169

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 182

Met Leu Ala Thr Arg Val Phe Ser Leu Val Gly Lys Arg Ala Ile Ser  
 1 5 10 15

Thr Ser Val Cys Val Arg Ala His Glu Ser Val Val Lys Ser Glu Asp  
 20 25 30

Phe Ser Leu Pro Ala Tyr Met Asp Arg Arg Asp His Pro Leu Pro Glu  
 35 40 45

Val Ala His Val Lys His Leu Ser Ala Ser Gln Lys Ala Leu Lys Glu  
 50 55 60

Lys Glu Lys Ala Ser Trp Ser Ser Leu Ser Met Asp Glu Lys Val Glu  
 65 70 75 80

Leu Tyr Arg Ile Lys Phe Lys Glu Ser Phe Ala Glu Met Asn Arg Gly  
 85 90 95

Ser Asn Glu Trp Lys Thr Val Val Gly Gly Ala Met Phe Phe Ile Gly  
 100 105 110

Phe Thr Ala Leu Val Ile Met Trp Gln Lys His Tyr Val Tyr Gly Pro  
 115 120 125

Leu Pro Gln Ser Phe Asp Lys Glu Trp Val Ala Lys Gln Thr Lys Arg  
 130 135 140

Met Leu Asp Met Lys Val Asn Pro Ile Gln Gly Leu Ala Ser Lys Trp  
 145 150 155 160

Asp Tyr Glu Lys Asn Glu Trp Lys Lys  
 165

&lt;210&gt; 183

&lt;211&gt; 879

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 183

Met Ala Gly Gly Gly Gly Asp Leu Ser Thr Arg Arg Leu Asn Glu Cys  
 1 5 10 15

Ile Ser Pro Val Ala Asn Glu Met Asn His Leu Pro Ala His Ser His  
 20 25 30

Asp Leu Gln Arg Met Phe Thr Glu Asp Gln Gly Val Asp Asp Arg Leu  
 35 40 45

Leu Tyr Asp Ile Val Phe Lys His Phe Lys Arg Asn Lys Val Glu Ile  
 50 55 60

Ser Asn Ala Ile Lys Lys Thr Phe Pro Phe Leu Glu Gly Leu Arg Asp  
 65 70 75 80

Arg Asp Leu Ile Thr Asn Lys Met Phe Glu Asp Ser Gln Asp Ser Cys  
 85 90 95



Arg Asn Leu Val Pro Val Gln Arg Val Val Tyr Asn Val Leu Ser Glu  
 100 105 110  
 Leu Glu Lys Thr Phe Asn Leu Pro Val Leu Glu Ala Leu Phe Ser Asp  
 115 120 125  
 Val Asn Met Gln Glu Tyr Pro Asp Leu Ile His Ile Tyr Lys Gly Phe  
 130 135 140  
 Glu Asn Val Ile His Asp Lys Leu Pro Leu Gln Glu Ser Glu Glu Glu  
 145 150 155 160  
 Glu Arg Glu Glu Arg Ser Gly Leu Gln Leu Ser Leu Glu Gln Gly Thr  
 165 170 175  
 Gly Glu Asn Ser Phe Arg Ser Leu Thr Trp Pro Pro Ser Gly Ser Pro  
 180 185 190  
 Ser His Ala Gly Thr Thr Pro Pro Glu Asn Gly Leu Ser Glu His Pro  
 195 200 205  
 Cys Glu Thr Glu Gln Ile Asn Ala Lys Arg Lys Asp Thr Thr Ser Asp  
 210 215 220  
 Lys Asp Asp Ser Leu Gly Ser Gln Gln Thr Asn Glu Gln Cys Ala Gln  
 225 230 235 240  
 Lys Ala Glu Pro Thr Glu Ser Cys Glu Gln Ile Ala Val Gln Val Asn  
 245 250 255  
 Asn Gly Asp Ala Gly Arg Glu Met Pro Cys Pro Leu Pro Cys Asp Glu  
 260 265 270  
 Glu Ser Pro Glu Ala Glu Leu His Asn His Gly Ile Gln Ile Asn Ser  
 275 280 285  
 Cys Ser Val Arg Leu Val Asp Ile Lys Lys Glu Lys Pro Phe Ser Asn  
 290 295 300  
 Ser Lys Val Glu Cys Gln Ala Gln Ala Arg Thr His His Asn Gln Ala  
 305 310 315 320  
 Ser Asp Ile Ile Val Ile Ser Ser Glu Asp Ser Glu Gly Ser Thr Asp  
 325 330 335  
 Val Asp Glu Pro Leu Glu Val Phe Ile Ser Ala Pro Arg Ser Glu Pro  
 340 345 350  
 Val Ile Asn Asn Asp Asn Pro Leu Glu Ser Asn Asp Glu Lys Glu Gly  
 355 360 365  
 Gln Glu Ala Thr Cys Ser Arg Pro Gln Ile Val Pro Glu Pro Met Asp  
 370 375 380  
 Phe Arg Lys Leu Ser Thr Phe Arg Glu Ser Phe Lys Lys Arg Val Ile  
 385 390 395 400  
 Gly Gln Asp His Asp Phe Ser Glu Ser Ser Glu Glu Glu Ala Pro Ala  
 405 410 415

Glu Ala Ser Ser Gly Ala Leu Arg Ser Lys His Gly Glu Lys Ala Pro  
 420 425 430  
 Met Thr Ser Arg Ser Thr Ser Thr Trp Arg Ile Pro Ser Arg Lys Arg  
 435 440 445  
 Arg Phe Ser Ser Ser Asp Phe Ser Asp Leu Ser Asn Gly Glu Glu Leu  
 450 455 460  
 Gln Glu Thr Cys Ser Ser Ser Leu Arg Arg Gly Ser Gly Ser Gln Pro  
 465 470 475 480  
 Gln Glu Pro Glu Asn Lys Lys Cys Ser Cys Val Met Cys Phe Pro Lys  
 485 490 495  
 Gly Val Pro Arg Ser Gln Glu Ala Arg Thr Glu Ser Ser Gln Ala Ser  
 500 505 510  
 Asp Met Met Asp Thr Met Asp Val Glu Asn Asn Ser Thr Leu Glu Lys  
 515 520 525  
 His Ser Gly Lys Arg Arg Lys Lys Arg Arg His Arg Ser Lys Val Asn  
 530 535 540  
 Gly Leu Gln Arg Gly Arg Lys Lys Asp Arg Pro Arg Lys His Leu Thr  
 545 550 555 560  
 Leu Asn Asn Lys Val Gln Lys Lys Arg Trp Gln Gln Arg Gly Arg Lys  
 565 570 575  
 Ala Asn Thr Arg Pro Leu Lys Arg Arg Arg Lys Arg Gly Pro Arg Ile  
 580 585 590  
 Pro Lys Asp Glu Asn Ile Asn Phe Lys Gln Ser Glu Leu Pro Val Thr  
 595 600 605  
 Cys Gly Glu Val Lys Gly Thr Leu Tyr Lys Glu Arg Phe Lys Gln Gly  
 610 615 620  
 Thr Ser Lys Lys Cys Ile Gln Ser Glu Asp Lys Lys Trp Phe Thr Pro  
 625 630 635 640  
 Arg Glu Phe Glu Ile Glu Gly Asp Arg Gly Ala Ser Lys Asn Trp Lys  
 645 650 655  
 Leu Ser Ile Arg Cys Gly Gly Tyr Thr Leu Lys Val Leu Met Glu Asn  
 660 665 670  
 Lys Phe Leu Pro Glu Pro Pro Ser Thr Arg Lys Lys Arg Ile Leu Glu  
 675 680 685  
 Ser His Asn Asn Thr Leu Val Asp Pro Cys Glu Glu His Lys Lys Lys  
 690 695 700  
 Asn Pro Asp Ala Ser Val Lys Phe Ser Glu Phe Leu Lys Lys Cys Ser  
 705 710 715 720  
 Glu Thr Trp Lys Thr Ile Phe Ala Lys Glu Lys Gly Lys Phe Glu Asp

[illegible]

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      130              135              140
Val Tyr Glu Gln Lys Ser Leu Lys Gly Arg Ala Asn Asp Ala Ile Ala
145              150              155              160

Ser Ala Cys Leu Tyr Ile Ala Cys Arg Gln Glu Gly Val Pro Arg Thr
      165              170              175

Phe Lys Glu Ile Cys Ala Val Ser Arg Ile Ser Lys Lys Glu Ile Gly
      180              185              190

Arg Cys Phe Lys Leu Ile Leu Lys Ala Leu Glu Thr Ser Val Asp Leu
      195              200              205

Ile Thr Thr Gly Asp Phe Met Ser Arg Phe Cys Ser Asn Leu Cys Leu
      210              215              220

Pro Lys Gln Val Gln Met Ala Ala Thr His Ile Ala Arg Lys Ala Val
      225              230              235              240

Glu Leu Asp Leu Val Pro Gly Arg Ser Pro Ile Ser Val Ala Ala Ala
      245              250              255

Ala Ile Tyr Met Ala Ser Gln Ala Ser Ala Glu Lys Arg Thr Gln Lys
      260              265              270

Glu Ile Gly Asp Ile Ala Gly Val Ala Asp Val Thr Ile Arg Gln Ser
      275              280              285

Tyr Arg Leu Ile Tyr Pro Arg Ala Pro Asp Leu Phe Pro Thr Asp Phe
      290              295              300

Lys Phe Asp Thr Pro Val Asp Lys Leu Pro Gln Leu
      305              310              315

<210> 185
<211> 628
<212> PRT
<213> Homo sapiens

<400> 185
Ala Asp Phe Leu Asp Ala Leu Ile Val Ser Met Asp Val Ile Gln His
1              5              10              15

Glu Thr Ile Gly Lys Lys Phe Glu Lys Arg His Ile Glu Ile Phe Thr
      20              25              30

Asp Leu Ser Ser Arg Phe Ser Lys Ser Gln Leu Asp Ile Ile Ile His
      35              40              45

Ser Leu Lys Lys Cys Asp Ile Ser Leu Gln Phe Phe Leu Pro Phe Ser
      50              55              60

Leu Gly Lys Glu Asp Gly Ser Gly Asp Arg Gly Asp Gly Pro Phe Arg
      65              70              75              80

Leu Gly Gly His Gly Pro Ser Phe Pro Leu Lys Gly Ile Thr Glu Gln
      85              90              95

Gln Lys Glu Gly Leu Glu Ile Val Lys Met Val Met Ile Ser Leu Glu

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100	105	110
Gly Glu Asp Gly Leu Asp Glu 115	Ile Tyr Ser Phe Ser 120	Glu Ser Leu Arg 125
Lys Leu Cys Val Phe Lys 130	Lys Ile Glu Arg His 135	Ser Ile His Trp Pro 140
Cys Arg Leu Thr Ile 145	Gly Ser Asn Leu Ser 150	Ile Arg Ile Ala Ala Tyr 155
Lys Ser Ile Leu Gln Glu Arg Val 165	Lys Thr Trp Thr Val 170	Val Asp 175
Ala Lys Thr Leu Lys Lys Glu Asp 180	Ile Gln Lys Glu Thr Val 185	Tyr Cys 190
Leu Asn Asp Asp Asp Glu Thr 195	Glu Val Leu Lys Glu Asp 200	Ile Ile Gln 205
Gly Phe Leu Tyr Gly Ser 210	Asp Ile Val Pro Phe Ser 215	Lys Val Asp Glu 220
Glu Gln Met Lys Tyr 225	Lys Ser Glu Gly Lys Cys Phe Ser Val Leu Gly 230	
Phe Cys Lys Ser Ser Gln Val Gln Arg Arg Phe Phe Met Gly Asn Gln 245		255
Val Leu Lys Val Phe Ala Ala Arg Asp Asp Glu Ala Ala Ala Val Ala 260		270
Leu Ser Ser Leu Ile His Ala Leu Asp Asp Leu Asp Met Val Ala Ile 275		285
Val Arg Tyr Ala Tyr Asp Lys Arg Ala Asn Pro Gln Val Gly Val Ala 290		300
Phe Pro His Ile Lys His Asn Tyr Glu Cys Leu Val Tyr Val Gln Leu 305		315
Pro Phe Met Glu Asp Leu Arg Gln Tyr Met Phe Ser Ser Leu Lys Asn 325		335
Ser Lys Lys Tyr Ala Pro Thr Glu Ala Gln Leu Asn Ala Val Asp Ala 340		350
Leu Ile Asp Ser Met Ser Leu Ala Lys Lys Asp Glu Lys Thr Asp Thr 355		365
Leu Glu Asp Leu Phe Pro Thr Thr Lys Ile Pro Asn Pro Arg Phe Gln 370		380
Arg Leu Phe Gln Cys Leu Leu His Arg Ala Leu His Pro Arg Glu Pro 385		395
Leu Pro Pro Ile Gln Gln His Ile Trp Asn Met Leu Asn Pro Pro Ala 405		415

Glu Val Thr Thr Lys Ser Gln Ile Pro Leu Ser Lys Ile Lys Thr Leu  
420 425 430

Phe Pro Leu Ile Glu Ala Lys Lys Lys Asp Gln Val Thr Ala Gln Glu  
435 440 445

Ile Phe Gln Asp Asn His Glu Asp Gly Pro Thr Ala Lys Lys Leu Lys  
450 455 460

Thr Glu Gln Gly Gly Ala His Phe Ser Val Ser Ser Leu Ala Glu Gly  
465 470 475 480

Ser Val Thr Ser Val Gly Ser Val Asn Pro Ala Glu Asn Phe Arg Val  
485 490 495

Leu Val Lys Gln Lys Lys Ala Ser Phe Glu Glu Ala Ser Asn Gln Leu  
500 505 510

Ile Asn His Ile Glu Gln Phe Leu Asp Thr Asn Glu Thr Pro Tyr Phe  
515 520 525

Met Lys Ser Ile Asp Cys Ile Arg Ala Phe Arg Glu Glu Ala Ile Lys  
530 535 540

Phe Ser Glu Glu Gln Arg Phe Asn Asn Phe Leu Lys Ala Leu Gln Glu  
545 550 555 560

Lys Val Glu Ile Lys Gln Leu Asn His Phe Trp Glu Ile Val Val Gln  
565 570 575

Asp Gly Ile Thr Leu Ile Thr Lys Glu Glu Ala Ser Gly Ser Ser Val  
580 585 590

Thr Ala Glu Glu Ala Lys Lys Phe Leu Ala Pro Lys Asp Lys Pro Ser  
595 600 605

Gly Asp Thr Ala Ala Val Phe Glu Glu Gly Gly Asp Val Asp Asp Leu  
610 615 620

Leu Asp Met Ile  
625

<210> 186  
<211> 420  
<212> PRT  
<213> Homo sapiens

<400> 186

Met Gly Ser Gly Trp Lys Lys Ile Lys Leu Gln Met Lys Cys Asp Gly  
1 5 10 15

Cys Ser Glu Gln Gly Ser His Pro Cys Ala Phe Ile Gly Ile Gly Asn  
20 25 30

Ser Asp Gln Glu Met Gln Gln Leu Asn Leu Glu Gly Lys Asn Tyr Cys  
35 40 45

Thr Ala Lys Thr Leu Tyr Ile Ser Asp Ser Asp Lys Gln Lys His Phe  
50 55 60

Met Leu Ser Val Lys Val Phe Tyr Gly Asn Gly Asp Asp Ile Gly Val  
 65 70 75 80  
 Phe Leu Ser Lys Ser Ser Lys Pro Ser Lys Lys Lys Gln Ser Leu Lys  
 85 90 95  
 Asn Ala Asp Leu Cys Ile Gly Ser Gly Thr Lys Val Ala Leu Phe Asn  
 100 105 110  
 Arg Leu Arg Ser Gln Thr Val Ser Thr Arg Tyr Leu His Val Glu Gly  
 115 120 125  
 Gly Asn Phe His Ala Ser Ser Gln Gln Trp Gly Ala Phe Thr Leu Phe  
 130 135 140  
 Leu Asp Asp Asp Gly Ser Glu Gly Glu Glu Phe Thr Val Arg Asp Gly  
 145 150 155 160  
 Tyr Ile His Tyr Gly Gln Thr Val Lys Leu Val Cys Ser Val Thr Gly  
 165 170 175  
 Met Ala Leu Pro Arg Leu Ile Ile Arg Lys Val Asp Lys Gln Thr Thr  
 180 185 190  
 Leu Leu Asp Ala Asp Asp Pro Val Ser Gln Leu His Lys Cys Ala Phe  
 195 200 205  
 Asp Leu Glu Asp Thr Glu Arg Met Tyr Leu Cys Leu Ser Gln Glu Arg  
 210 215 220  
 Ile Ile Gln Phe Gln Ala Thr Pro Cys Pro Thr Glu Pro Asn Lys Glu  
 225 230 235 240  
 Met Ile Asn Asp Gly Ala Ser Trp Ala Ile Ile Ser Thr His Lys Ala  
 245 250 255  
 Lys Tyr Thr Phe Tyr Glu Arg Met Gly Pro Val Leu Ala Leu Val Met  
 260 265 270  
 Pro Met Pro Val Val Glu Ser Leu Lys Leu Asn Gly Gly Gly Asp Glu  
 275 280 285  
 Ala Met Leu Glu Leu Thr Gly Gln Asn Phe Thr Pro Asn Leu Arg Val  
 290 295 300  
 Trp Phe Gly Asp Val Glu Ala Glu Thr Met Tyr Arg Cys Gly Glu Ser  
 305 310 315 320  
 Met Leu Arg Val Val Pro Asp Val Leu His Ser Glu Lys Val Gly Asp  
 325 330 335  
 Ser Ser Gln Gln Pro Val Gln Val Ser Val Thr Leu Val Arg Asn Asp  
 340 345 350  
 Gly Ile Ile Tyr Ser Thr Ser Leu Thr Phe Thr Tyr Thr Pro Glu Ala  
 355 360 365  
 Gly Pro Arg Pro His Cys Ser Val Ala Gly Ala Ile Leu Lys Ala Ser  
 370 375 380

Ser Ser His Val Pro Pro Asn Glu Leu Asn Thr Asn Ser Asp Gly Ser  
385 390 395 400

Tyr Thr Asn Ala Ser Thr Asn Ser Thr Ser Val Thr Ser Ser Thr Pro  
405 410 415

Thr Val Val Ser  
420

<210> 187  
<211> 103  
<212> PRT  
<213> Homo sapiens

<400> 187

Met Glu Thr Val Gln Glu Leu Ile Pro Leu Ala Lys Glu Met Met Ala  
1 5 10 15

Gln Lys Arg Lys Gly Lys Met Val Lys Leu Tyr Val Leu Gly Ser Val  
20 25 30

Leu Ala Leu Phe Gly Val Val Leu Gly Leu Met Glu Thr Val Cys Ser  
35 40 45

Pro Phe Thr Ala Ala Arg Arg Leu Arg Asp Gln Glu Ala Ala Val Ala  
50 55 60

Glu Leu Gln Ala Ala Leu Glu Arg Gln Ala Leu Gln Lys Gln Ala Leu  
65 70 75 80

Gln Glu Lys Gly Lys Gln Gln Asp Thr Val Leu Gly Gly Arg Ala Leu  
85 90 95

Ser Asn Arg Gln His Ala Ser  
100

<210> 188  
<211> 1306  
<212> PRT  
<213> Homo sapiens

<400> 188

Met Gly Ala Ala Ser Gly Arg Arg Gly Pro Gly Leu Leu Leu Pro Leu  
1 5 10 15

Pro Leu Leu Leu Leu Leu Pro Pro Gln Pro Ala Leu Ala Leu Asp Pro  
20 25 30

Gly Leu Gln Pro Gly Asn Phe Ser Ala Asp Glu Ala Gly Ala Gln Leu  
35 40 45

Phe Ala Gln Ser Tyr Asn Ser Ser Ala Glu Gln Val Leu Phe Gln Ser  
50 55 60

Val Ala Ala Ser Trp Ala His Asp Thr Asn Ile Thr Ala Glu Asn Ala  
65 70 75 80

Arg Arg Gln Glu Glu Ala Ala Leu Leu Ser Gln Glu Phe Ala Glu Ala  
85 90 95



Trp Gly Gln Lys Ala Lys Glu Leu Tyr Glu Pro Ile Trp Gln Asn Phe  
 100 105 110  
 Thr Asp Pro Gln Leu Arg Arg Ile Ile Gly Ala Val Arg Thr Leu Gly  
 115 120 125  
 Ser Ala Asn Leu Pro Leu Ala Lys Arg Gln Gln Tyr Asn Ala Leu Leu  
 130 135 140  
 Ser Asn Met Ser Arg Ile Tyr Ser Thr Ala Lys Val Cys Leu Pro Asn  
 145 150 155 160  
 Lys Thr Ala Thr Cys Trp Ser Leu Asp Pro Asp Leu Thr Asn Ile Leu  
 165 170 175  
 Ala Ser Ser Arg Ser Tyr Ala Met Leu Leu Phe Ala Trp Glu Gly Trp  
 180 185 190  
 His Asn Ala Ala Gly Ile Pro Leu Lys Pro Leu Tyr Glu Asp Phe Thr  
 195 200 205  
 Ala Leu Ser Asn Glu Ala Tyr Lys Gln Asp Gly Phe Thr Asp Thr Gly  
 210 215 220  
 Ala Tyr Trp Arg Ser Trp Tyr Asn Ser Pro Thr Phe Glu Asp Asp Leu  
 225 230 235 240  
 Glu His Leu Tyr Gln Gln Leu Glu Pro Leu Tyr Leu Asn Leu His Ala  
 245 250 255  
 Phe Val Arg Arg Ala Leu His Arg Arg Tyr Gly Asp Arg Tyr Ile Asn  
 260 265 270  
 Leu Arg Gly Pro Ile Pro Ala His Leu Leu Gly Asp Met Trp Ala Gln  
 275 280 285  
 Ser Trp Glu Asn Ile Tyr Asp Met Val Val Pro Phe Pro Asp Lys Pro  
 290 295 300  
 Asn Leu Asp Val Thr Ser Thr Met Leu Gln Gln Gly Trp Asn Ala Thr  
 305 310 315 320  
 His Met Phe Arg Val Ala Glu Glu Phe Phe Thr Ser Leu Glu Leu Ser  
 325 330 335  
 Pro Met Pro Pro Glu Phe Trp Glu Gly Ser Met Leu Glu Lys Pro Ala  
 340 345 350  
 Asp Gly Arg Glu Val Val Cys His Ala Ser Ala Trp Asp Phe Tyr Asn  
 355 360 365  
 Arg Lys Asp Phe Arg Ile Lys Gln Cys Thr Arg Val Thr Met Asp Gln  
 370 375 380  
 Leu Ser Thr Val His His Glu Met Gly His Ile Gln Tyr Tyr Leu Gln  
 385 390 395 400  
 Tyr Lys Asp Leu Pro Val Ser Leu Arg Arg Gly Ala Asn Pro Gly Phe  
 405 410 415

His Glu Ala Ile Gly Asp Val Leu Ala Leu Ser Val Ser Thr Pro Glu  
 420 425 430  
 His Leu His Lys Ile Gly Leu Leu Asp Arg Val Thr Asn Asp Thr Glu  
 435 440 445  
 Ser Asp Ile Asn Tyr Leu Leu Lys Met Ala Leu Glu Lys Ile Ala Phe  
 450 455 460  
 Leu Pro Phe Gly Tyr Leu Val Asp Gln Trp Arg Trp Gly Val Phe Ser  
 465 470 475 480  
 Gly Arg Thr Pro Pro Ser Arg Tyr Asn Phe Asp Trp Trp Tyr Leu Arg  
 485 490 495  
 Thr Lys Tyr Gln Gly Ile Cys Pro Pro Val Thr Arg Asn Glu Thr His  
 500 505 510  
 Phe Asp Ala Gly Ala Lys Phe His Val Pro Asn Val Thr Pro Tyr Ile  
 515 520 525  
 Arg Tyr Phe Val Ser Phe Val Leu Gln Phe Gln Phe His Glu Ala Leu  
 530 535 540  
 Cys Lys Glu Ala Gly Tyr Glu Gly Pro Leu His Gln Cys Asp Ile Tyr  
 545 550 555 560  
 Arg Ser Thr Lys Ala Gly Ala Lys Leu Arg Lys Val Leu Gln Ala Gly  
 565 570 575  
 Ser Ser Arg Pro Trp Gln Glu Val Leu Lys Asp Met Val Gly Leu Asp  
 580 585 590  
 Ala Leu Asp Ala Gln Pro Leu Leu Lys Tyr Phe Gln Pro Val Thr Gln  
 595 600 605  
 Trp Leu Gln Glu Gln Asn Gln Gln Asn Gly Glu Val Leu Gly Trp Pro  
 610 615 620  
 Glu Tyr Gln Trp His Pro Pro Leu Pro Asp Asn Tyr Pro Glu Gly Ile  
 625 630 635 640  
 Asp Leu Val Thr Asp Glu Ala Glu Ala Ser Lys Phe Val Glu Glu Tyr  
 645 650 655  
 Asp Arg Thr Ser Gln Val Val Trp Asn Glu Tyr Ala Glu Ala Asn Trp  
 660 665 670  
 Asn Tyr Asn Thr Asn Ile Thr Thr Glu Thr Ser Lys Ile Leu Leu Gln  
 675 680 685  
 Lys Asn Met Gln Ile Ala Asn His Thr Leu Lys Tyr Gly Thr Gln Ala  
 690 695 700  
 Arg Lys Phe Asp Val Asn Gln Leu Gln Asn Thr Thr Ile Lys Arg Ile  
 705 710 715 720  
 Ile Lys Lys Val Gln Asp Leu Glu Arg Ala Ala Leu Pro Ala Gln Glu  
 725 730 735

Leu Glu Glu Tyr Asn Lys Ile Leu Leu Asp Met Glu Thr Thr Tyr Ser  
 740 745 750  
 Val Ala Thr Val Cys His Pro Asn Gly Ser Cys Leu Gln Leu Glu Pro  
 755 760 765  
 Asp Leu Thr Asn Val Met Ala Thr Ser Arg Lys Tyr Glu Asp Leu Leu  
 770 775 780  
 Trp Ala Trp Glu Gly Trp Arg Asp Lys Ala Gly Arg Ala Ile Leu Gln  
 785 790 795 800  
 Phe Tyr Pro Lys Tyr Val Glu Leu Ile Asn Gln Ala Ala Arg Leu Asn  
 805 810 815  
 Gly Tyr Val Asp Ala Gly Asp Ser Trp Arg Ser Met Tyr Glu Thr Pro  
 820 825 830  
 Ser Leu Glu Gln Asp Leu Glu Arg Leu Phe Gln Glu Leu Gln Pro Leu  
 835 840 845  
 Tyr Leu Asn Leu His Ala Tyr Val Arg Arg Ala Leu His Arg His Tyr  
 850 855 860  
 Gly Ala Gln His Ile Asn Leu Glu Gly Pro Ile Pro Ala His Leu Leu  
 865 870 875 880  
 Gly Asn Met Trp Ala Gln Thr Trp Ser Asn Ile Tyr Asp Leu Val Val  
 885 890 895  
 Pro Phe Pro Ser Ala Pro Ser Met Asp Thr Thr Glu Ala Met Leu Lys  
 900 905 910  
 Gln Gly Trp Thr Pro Arg Arg Met Phe Lys Glu Ala Asp Asp Phe Phe  
 915 920 925  
 Thr Ser Leu Gly Leu Leu Pro Val Pro Pro Glu Phe Trp Asn Lys Ser  
 930 935 940  
 Met Leu Glu Lys Pro Thr Asp Gly Arg Glu Val Val Cys His Ala Ser  
 945 950 955 960  
 Ala Trp Asp Phe Tyr Asn Gly Lys Asp Phe Arg Ile Lys Gln Cys Thr  
 965 970 975  
 Thr Val Asn Leu Glu Asp Leu Val Val Ala His His Glu Met Gly His  
 980 985 990  
 Ile Gln Tyr Phe Met Gln Tyr Lys Asp Leu Pro Val Ala Leu Arg Glu  
 995 1000 1005  
 Gly Ala Asn Pro Gly Phe His Glu Ala Ile Gly Asp Val Leu Ala  
 1010 1015 1020  
 Leu Ser Val Ser Thr Pro Lys His Leu His Ser Leu Asn Leu Leu  
 1025 1030 1035  
 Ser Ser Glu Gly Gly Ser Asp Glu His Asp Ile Asn Phe Leu Met

1040	1045	1050
Lys Met 1055	Ala Leu Asp Lys Ile 1060	Ala Phe Ile Pro Phe Ser Tyr Leu 1065
Val Asp 1070	Gln Trp Arg Trp Arg 1075	Val Phe Asp Gly Ser Ile Thr Lys 1080
Glu Asn 1085	Tyr Asn Gln Glu Trp 1090	Trp Ser Leu Arg Leu Lys Tyr Gln 1095
Gly Leu 1100	Cys Pro Pro Val Pro 1105	Arg Thr Gln Gly Asp Phe Asp Pro 1110
Gly Ala 1115	Lys Phe His Ile Pro 1120	Ser Ser Val Pro Tyr Ile Arg Tyr 1125
Phe Val 1130	Ser Phe Ile Ile Gln 1135	Phe Gln Phe His Glu Ala Leu Cys 1140
Gln Ala 1145	Ala Gly His Thr Gly 1150	Pro Leu His Lys Cys Asp Ile Tyr 1155
Gln Ser 1160	Lys Glu Ala Gly Gln 1165	Arg Leu Ala Thr Ala Met Lys Leu 1170
Gly Phe 1175	Ser Arg Pro Trp Pro 1180	Glu Ala Met Gln Leu Ile Thr Gly 1185
Gln Pro 1190	Asn Met Ser Ala Ser 1195	Ala Met Leu Ser Tyr Phe Lys Pro 1200
Leu Leu 1205	Asp Trp Leu Arg Thr 1210	Glu Asn Glu Leu His Gly Glu Lys 1215
Leu Gly 1220	Trp Pro Gln Tyr Asn 1225	Trp Thr Pro Asn Ser Ala Arg Ser 1230
Glu Gly 1235	Pro Leu Pro Asp Ser 1240	Gly Arg Val Ser Phe Leu Gly Leu 1245
Asp Leu 1250	Asp Ala Gln Gln Ala 1255	Arg Val Gly Gln Trp Leu Leu Leu 1260
Phe Leu 1265	Gly Ile Ala Leu Leu 1270	Val Ala Thr Leu Gly Leu Ser Gln 1275
Arg Leu 1280	Phe Ser Ile Arg His 1285	Arg Ser Leu His Arg His Ser His 1290
Gly Pro 1295	Gln Phe Gly Ser Glu 1300	Val Glu Leu Arg His Ser 1305

<210> 189  
 <211> 1461  
 <212> PRT  
 <213> Homo sapiens

<400> 189

Met Ala Ala Glu Arg Gly Ala Arg Arg Leu Leu Ser Thr Pro Ser Phe

1	5	10	15												
Trp	Leu	Tyr	Cys	Leu	Leu	Leu	Leu	Gly	Arg	Arg	Ala	Pro	Gly	Ala	Ala
	20							25					30		
Ala	Ala	Arg	Ser	Gly	Ser	Ala	Pro	Gln	Ser	Pro	Gly	Ala	Ser	Ile	Arg
	35						40					45			
Thr	Phe	Thr	Pro	Phe	Tyr	Phe	Leu	Val	Glu	Pro	Val	Asp	Thr	Leu	Ser
	50					55					60				
Val	Arg	Gly	Ser	Ser	Val	Ile	Leu	Asn	Cys	Ser	Ala	Tyr	Ser	Glu	Pro
65					70					75					80
Ser	Pro	Lys	Ile	Glu	Trp	Lys	Lys	Asp	Gly	Thr	Phe	Leu	Asn	Leu	Val
				85					90					95	
Ser	Asp	Asp	Arg	Arg	Gln	Leu	Leu	Pro	Asp	Gly	Ser	Leu	Phe	Ile	Ser
			100					105						110	
Asn	Val	Val	His	Ser	Lys	His	Asn	Lys	Pro	Asp	Glu	Gly	Tyr	Tyr	Gln
		115					120					125			
Cys	Val	Ala	Thr	Val	Glu	Ser	Leu	Gly	Thr	Ile	Ile	Ser	Arg	Thr	Ala
	130					135					140				
Lys	Leu	Ile	Val	Ala	Gly	Leu	Pro	Arg	Phe	Thr	Ser	Gln	Pro	Glu	Pro
145					150					155					160
Ser	Ser	Val	Tyr	Ala	Gly	Asn	Gly	Ala	Ile	Leu	Asn	Cys	Glu	Val	Asn
				165					170					175	
Ala	Asp	Leu	Val	Pro	Phe	Val	Arg	Trp	Glu	Gln	Asn	Arg	Gln	Pro	Leu
		180						185						190	
Leu	Leu	Asp	Asp	Arg	Val	Ile	Lys	Leu	Pro	Ser	Gly	Met	Leu	Val	Ile
		195					200					205			
Ser	Asn	Ala	Thr	Glu	Gly	Asp	Gly	Gly	Leu	Tyr	Arg	Cys	Val	Val	Glu
	210					215					220				
Ser	Gly	Gly	Pro	Pro	Lys	Tyr	Ser	Asp	Glu	Val	Glu	Leu	Lys	Val	Leu
225					230					235					240
Pro	Asp	Pro	Glu	Val	Ile	Ser	Asp	Leu	Val	Phe	Leu	Lys	Gln	Pro	Ser
			245						250					255	
Pro	Leu	Val	Arg	Val	Ile	Gly	Gln	Asp	Val	Val	Leu	Pro	Cys	Val	Ala
		260						265					270		
Ser	Gly	Leu	Pro	Thr	Pro	Thr	Ile	Lys	Trp	Met	Lys	Asn	Glu	Glu	Ala
		275					280					285			
Leu	Asp	Thr	Glu	Ser	Ser	Glu	Arg	Leu	Val	Leu	Leu	Ala	Gly	Gly	Ser
	290					295					300				
Leu	Glu	Ile	Ser	Asp	Val	Thr	Glu	Asp	Asp	Ala	Gly	Thr	Tyr	Phe	Cys
305					310					315					320

Ile Ala Asp Asn Gly Asn Glu Thr Ile Glu Ala Gln Ala Glu Leu Thr  
 325 330 335  
 Val Gln Ala Gln Pro Glu Phe Leu Lys Gln Pro Thr Asn Ile Tyr Ala  
 340 345 350  
 His Glu Ser Met Asp Ile Val Phe Glu Cys Glu Val Thr Gly Lys Pro  
 355 360 365  
 Thr Pro Thr Val Lys Trp Val Lys Asn Gly Asp Met Val Ile Pro Ser  
 370 375 380  
 Asp Tyr Phe Lys Ile Val Lys Glu His Asn Leu Gln Val Leu Gly Leu  
 385 390 395 400  
 Val Lys Ser Asp Glu Gly Phe Tyr Gln Cys Ile Ala Glu Asn Asp Val  
 405 410 415  
 Gly Asn Ala Gln Ala Gly Ala Gln Leu Ile Ile Leu Glu His Ala Pro  
 420 425 430  
 Ala Thr Thr Gly Pro Leu Pro Ser Ala Pro Arg Asp Val Val Ala Ser  
 435 440 445  
 Leu Val Ser Thr Arg Phe Ile Lys Leu Thr Trp Arg Thr Pro Ala Ser  
 450 455 460  
 Asp Pro His Gly Asp Asn Leu Thr Tyr Ser Val Phe Tyr Thr Lys Glu  
 465 470 475 480  
 Gly Ile Ala Arg Glu Arg Val Glu Asn Thr Ser His Pro Gly Glu Met  
 485 490 495  
 Gln Val Thr Ile Gln Asn Leu Met Pro Ala Thr Val Tyr Ile Phe Arg  
 500 505 510  
 Val Met Ala Gln Asn Lys His Gly Ser Gly Glu Ser Ser Ala Pro Leu  
 515 520 525  
 Arg Val Glu Thr Gln Pro Glu Val Gln Leu Pro Gly Pro Ala Pro Asn  
 530 535 540  
 Leu Arg Ala Tyr Ala Ala Ser Pro Thr Ser Ile Thr Val Thr Trp Glu  
 545 550 555 560  
 Thr Pro Val Ser Gly Asn Gly Glu Ile Gln Asn Tyr Lys Leu Tyr Tyr  
 565 570 575  
 Met Glu Lys Gly Thr Asp Lys Glu Gln Asp Val Asp Val Ser Ser His  
 580 585 590  
 Ser Tyr Thr Ile Asn Gly Leu Lys Lys Tyr Thr Glu Tyr Ser Phe Arg  
 595 600 605  
 Val Val Ala Tyr Asn Lys His Gly Pro Gly Val Ser Thr Pro Asp Val  
 610 615 620  
 Ala Val Arg Thr Leu Ser Asp Val Pro Ser Ala Ala Pro Gln Asn Leu  
 625 630 635 640

Ser Leu Glu Val Arg Asn Ser Lys Ser Ile Met Ile His Trp Gln Pro  
 645 650 655  
 Pro Ala Pro Ala Thr Gln Asn Gly Gln Ile Thr Gly Tyr Lys Ile Arg  
 660 665 670  
 Tyr Arg Lys Ala Ser Arg Lys Ser Asp Val Thr Glu Thr Leu Val Ser  
 675 680 685  
 Gly Thr Gln Leu Ser Gln Leu Ile Glu Gly Leu Asp Arg Gly Thr Glu  
 690 695 700  
 Tyr Asn Phe Arg Val Ala Ala Leu Thr Ile Asn Gly Thr Gly Pro Ala  
 705 710 715 720  
 Thr Asp Trp Leu Ser Ala Glu Thr Phe Glu Ser Asp Leu Asp Glu Thr  
 725 730 735  
 Arg Val Pro Glu Val Pro Ser Ser Leu His Val Arg Pro Leu Val Thr  
 740 745 750  
 Ser Ile Val Val Ser Trp Thr Pro Pro Glu Asn Gln Asn Ile Val Val  
 755 760 765  
 Arg Gly Tyr Ala Ile Gly Tyr Gly Ile Gly Ser Pro His Ala Gln Thr  
 770 775 780  
 Ile Lys Val Asp Tyr Lys Gln Arg Tyr Tyr Thr Ile Glu Asn Leu Asp  
 785 790 795 800  
 Pro Ser Ser His Tyr Val Ile Thr Leu Lys Ala Phe Asn Asn Val Gly  
 805 810 815  
 Glu Gly Ile Pro Leu Tyr Glu Ser Ala Val Thr Arg Pro His Thr Asp  
 820 825 830  
 Thr Ser Glu Val Asp Leu Phe Val Ile Asn Ala Pro Tyr Thr Pro Val  
 835 840 845  
 Pro Asp Pro Thr Pro Met Met Pro Pro Val Gly Val Gln Ala Ser Ile  
 850 855 860  
 Leu Ser His Asp Thr Ile Arg Ile Thr Trp Ala Asp Asn Ser Leu Pro  
 865 870 875 880  
 Lys His Gln Lys Ile Thr Asp Ser Arg Tyr Tyr Thr Val Arg Trp Lys  
 885 890 895  
 Thr Asn Ile Pro Ala Asn Thr Lys Tyr Lys Asn Ala Asn Ala Thr Thr  
 900 905 910  
 Leu Ser Tyr Leu Val Thr Gly Leu Lys Pro Asn Thr Leu Tyr Glu Phe  
 915 920 925  
 Ser Val Met Val Thr Lys Gly Arg Arg Ser Ser Thr Trp Ser Met Thr  
 930 935 940  
 Ala His Gly Thr Thr Phe Glu Leu Val Pro Thr Ser Pro Pro Lys Asp  
 945 950 955 960

Val Thr Val Val Ser Lys Glu Gly Lys Pro Lys Thr Ile Ile Val Asn  
 965 970 975  
 Trp Gln Pro Pro Ser Glu Ala Asn Gly Lys Ile Thr Gly Tyr Ile Ile  
 980 985 990  
 Tyr Tyr Ser Thr Asp Val Asn Ala Glu Ile His Asp Trp Val Ile Glu  
 995 1000 1005  
 Pro Val Val Gly Asn Arg Leu Thr His Gln Ile Gln Glu Leu Thr  
 1010 1015 1020  
 Leu Asp Thr Pro Tyr Tyr Phe Lys Ile Gln Ala Arg Asn Ser Lys  
 1025 1030 1035  
 Gly Met Gly Pro Met Ser Glu Ala Val Gln Phe Arg Thr Pro Lys  
 1040 1045 1050  
 Ala Asp Ser Ser Asp Lys Met Pro Asn Asp Gln Ala Ser Gly Ser  
 1055 1060 1065  
 Gly Gly Lys Gly Ser Arg Leu Pro Asp Leu Gly Ser Asp Tyr Lys  
 1070 1075 1080  
 Pro Pro Met Ser Gly Ser Asn Ser Pro His Gly Ser Pro Thr Ser  
 1085 1090 1095  
 Pro Leu Asp Ser Asn Met Leu Leu Val Ile Ile Val Ser Val Gly  
 1100 1105 1110  
 Val Ile Thr Ile Val Val Val Val Ile Ile Ala Val Phe Cys Thr  
 1115 1120 1125  
 Arg Arg Thr Thr Ser His Gln Lys Lys Lys Arg Ala Ala Cys Lys  
 1130 1135 1140  
 Ser Val Asn Gly Ser His Lys Tyr Lys Gly Asn Ser Lys Asp Val  
 1145 1150 1155  
 Lys Pro Pro Asp Leu Trp Ile His His Glu Arg Leu Glu Leu Lys  
 1160 1165 1170  
 Pro Ile Asp Lys Ser Pro Asp Pro Asn Pro Ile Met Thr Asp Thr  
 1175 1180 1185  
 Pro Ile Pro Arg Asn Ser Gln Asp Ile Thr Pro Val Asp Asn Ser  
 1190 1195 1200  
 Met Asp Ser Asn Ile His Gln Arg Arg Asn Ser Tyr Arg Gly His  
 1205 1210 1215  
 Glu Ser Glu Asp Ser Met Ser Thr Leu Ala Gly Arg Arg Gly Met  
 1220 1225 1230  
 Arg Pro Lys Met Met Met Pro Phe Asp Ser Gln Pro Pro Gln Pro  
 1235 1240 1245  
 Val Ile Ser Ala His Pro Ile His Ser Leu Asp Asn Pro His His



1250                      1255                      1260  
 His Phe His Ser Ser Ser Leu Ala Ser Pro Ala Arg Ser His Leu  
 1265                      1270                      1275  
 Tyr His Pro Gly Ser Pro Trp Pro Ile Gly Thr Ser Met Ser Leu  
 1280                      1285                      1290  
 Ser Asp Arg Ala Asn Ser Thr Glu Ser Val Arg Asn Thr Pro Ser  
 1295                      1300                      1305  
 Thr Asp Thr Met Pro Ala Ser Ser Ser Gln Thr Cys Cys Thr Asp  
 1310                      1315                      1320  
 His Gln Asp Pro Glu Gly Ala Thr Ser Ser Ser Tyr Leu Ala Ser  
 1325                      1330                      1335  
 Ser Gln Glu Glu Asp Ser Gly Gln Ser Leu Pro Thr Ala His Val  
 1340                      1345                      1350  
 Arg Pro Ser His Pro Leu Lys Ser Phe Ala Val Pro Ala Ile Pro  
 1355                      1360                      1365  
 Pro Pro Gly Pro Pro Thr Tyr Asp Pro Ala Leu Pro Ser Thr Pro  
 1370                      1375                      1380  
 Leu Leu Ser Gln Gln Ala Leu Asn His His Ile His Ser Val Lys  
 1385                      1390                      1395  
 Thr Ala Ser Ile Gly Thr Leu Gly Arg Ser Arg Pro Pro Met Pro  
 1400                      1405                      1410  
 Val Val Val Pro Ser Ala Pro Glu Val Gln Glu Thr Thr Arg Met  
 1415                      1420                      1425  
 Leu Glu Asp Ser Glu Ser Ser Tyr Glu Pro Asp Glu Leu Thr Lys  
 1430                      1435                      1440  
 Glu Met Ala His Leu Glu Gly Leu Met Lys Asp Leu Asn Ala Ile  
 1445                      1450                      1455  
 Thr Thr Ala  
 1460

<210> 190  
 <211> 736  
 <212> PRT  
 <213> Homo sapiens

<400> 190

Met Val Val Thr Arg Ser Ala Arg Ala Lys Ala Ser Ile Gln Ala Ala  
 1                      5                      10                      15

Ser Ala Glu Ser Ser Gly Gln Lys Ser Phe Ala Ala Asn Gly Ile Gln  
 20                      25                      30

Ala His Pro Glu Ser Ser Thr Gly Ser Asp Ala Arg Thr Thr Asp Glu  
 35                      40                      45

Ser Gln Thr Thr Gly Lys Gln Ser Leu Ile Pro Arg Thr Pro Lys Ala

50	55	60
Arg Lys Ser Lys Ser 65	Arg Thr Thr Gly Ser 70	Leu Pro Lys Gly Thr Glu 75 80
Pro Ser Thr Asp Gly 85	Glu Thr Ser Glu 90	Ala Glu Ser Asn Tyr Ser Val 95
Ser Glu His His 100	Asp Thr Ile Leu 105	Arg Val Thr Arg Arg Arg Gln Ile 110
Leu Ile Ala Cys Ser 115	Pro Val Ser Ser 120	Val Arg Lys Lys Pro Lys Val 125
Thr Pro Thr Lys Glu 130	Ser Tyr Thr Glu 135	Glu Glu Ile Val Ser Glu Ala Glu 140
Ser His Val Ser Gly 145	Ile Ser Arg Ile 150	Val Leu Pro Thr Glu Lys Thr 155 160
Thr Gly Ala Arg Arg 165	Ser Lys Ala Lys 170	Ser Leu Thr Asp Pro Ser Gln 175
Glu Ser His Thr Glu 180	Ala Ile Ser Asp 185	Ala Glu Thr Ser Ser Ser Asp 190
Ile Ser Phe Ser Gly 195	Ile Ala Thr Arg 200	Arg Thr Arg Ser Met Gln Arg 205
Lys Leu Lys Ala Gln 210	Thr Glu Lys Lys 215	Asp Ser Lys Ile Val Pro Gly 220
Asn Glu Lys Gln Ile 225	Val Gly Thr Pro 230	Val Asn Ser Glu Asp Ser Asp 235 240
Thr Arg Gln Thr Ser 245	His Leu Gln Ala 250	Arg Ser Leu Ser Glu Ile Asn 255
Lys Pro Asn Phe Tyr 260	Asn Asn Asp Phe 265	Asp Asp Asp Phe Ser His Arg 270
Ser Ser Glu Asn Ile 275	Leu Thr Val His 280	Glu Gln Ala Asn Val Glu Ser 285
Leu Lys Glu Thr Lys 290	Gln Asn Cys Lys 295	Asp Leu Asp Glu Asp Ala Asn 300
Gly Ile Thr Asp Glu 305	Gly Lys Glu Ile 310	Asn Glu Lys Ser Ser Gln Leu 315 320
Lys Asn Leu Ser Glu 325	Leu Gln Asp Thr 330	Ser Leu Gln Gln Leu Val Ser 335
Gln Arg His Ser Thr 340	Pro Gln Asn Lys 345	Asn Ala Val Ser Val His Ser 350
Asn Leu Asn Ser Glu 355	Ala Val Met Lys 360	Ser Leu Thr Gln Thr Phe Ala 365

Thr Val Glu Val Gly Arg Trp Asn Asn Asn Lys Lys Ser Pro Ile Lys  
 370 375 380  
 Ala Ser Asp Leu Thr Lys Phe Gly Asp Cys Gly Gly Ser Asp Asp Glu  
 385 390 395 400  
 Glu Glu Ser Thr Val Ile Ser Val Ser Glu Asp Met Asn Ser Glu Gly  
 405 410 415  
 Asn Val Asp Phe Glu Cys Asp Thr Lys Leu Tyr Thr Ser Ala Pro Asn  
 420 425 430  
 Thr Ser Gln Gly Lys Asp Asn Ser Val Leu Leu Val Leu Ser Ser Asp  
 435 440 445  
 Glu Ser Gln Gln Ser Glu Asn Ser Glu Asn Glu Glu Asp Thr Leu Cys  
 450 455 460  
 Phe Val Glu Asn Ser Gly Gln Arg Glu Ser Leu Ser Gly Asp Thr Gly  
 465 470 475 480  
 Ser Leu Ser Cys Asp Asn Ala Leu Phe Val Ile Asp Thr Thr Pro Gly  
 485 490 495  
 Met Ser Ala Asp Lys Asn Phe Tyr Leu Glu Glu Glu Asp Lys Ala Ser  
 500 505 510  
 Glu Val Ala Ile Glu Glu Glu Lys Glu Glu Glu Glu Asp Glu Lys Ser  
 515 520 525  
 Glu Glu Asp Ser Ser Asp His Asp Glu Asn Glu Asp Glu Phe Ser Asp  
 530 535 540  
 Glu Glu Asp Phe Leu Asn Ser Thr Lys Ala Lys Leu Leu Lys Leu Thr  
 545 550 555 560  
 Ser Ser Ser Ile Asp Pro Gly Leu Ser Ile Lys Gln Leu Gly Gly Leu  
 565 570 575  
 Tyr Ile Asn Phe Asn Ala Asp Lys Leu Gln Ser Asn Lys Arg Thr Leu  
 580 585 590  
 Thr Gln Ile Lys Glu Lys Lys Lys Asn Glu Leu Leu Gln Lys Ala Val  
 595 600 605  
 Ile Thr Pro Asp Phe Glu Lys Asn His Cys Val Pro Pro Tyr Ser Glu  
 610 615 620  
 Ser Lys Tyr Gln Leu Gln Lys Lys Arg Arg Lys Glu Arg Gln Lys Thr  
 625 630 635 640  
 Ala Gly Asp Gly Trp Phe Gly Met Lys Ala Pro Glu Met Thr Asn Glu  
 645 650 655  
 Leu Lys Asn Asp Leu Lys Ala Leu Lys Met Arg Ala Ser Met Asp Pro  
 660 665 670  
 Lys Arg Phe Tyr Lys Lys Asn Asp Arg Asp Gly Phe Pro Lys Tyr Phe  
 675 680 685

Gln Ile Gly Thr Ile Val Asp Asn Pro Ala Asp Phe Tyr His Ser Arg  
690 695 700

Ile Pro Lys Lys Gln Arg Lys Arg Thr Ile Val Glu Asp Cys Trp Leu  
705 710 715 720

Ile Leu Asn Ser Glu Ile Gln Pro Lys Glu Val Leu Arg Asp His Gly  
725 730 735

<210> 191  
<211> 465  
<212> PRT  
<213> Homo sapiens

<400> 191

Met Ala Met Thr Gly Ser Thr Pro Cys Ser Ser Met Ser Asn His Thr  
1 5 10 15

Lys Glu Arg Val Thr Met Thr Lys Val Thr Leu Glu Asn Phe Tyr Ser  
20 25 30

Asn Leu Ile Ala Gln His Glu Glu Arg Glu Met Arg Gln Lys Lys Leu  
35 40 45

Glu Lys Val Met Glu Glu Glu Gly Leu Lys Asp Glu Glu Lys Arg Leu  
50 55 60

Arg Arg Ser Ala His Ala Arg Lys Glu Thr Glu Phe Leu Arg Leu Lys  
65 70 75 80

Arg Thr Arg Leu Gly Leu Glu Asp Phe Glu Ser Leu Lys Val Ile Gly  
85 90 95

Arg Gly Ala Phe Gly Glu Val Arg Leu Val Gln Lys Lys Asp Thr Gly  
100 105 110

His Val Tyr Ala Met Lys Ile Leu Arg Lys Ala Asp Met Leu Glu Lys  
115 120 125

Glu Gln Val Gly His Ile Arg Ala Glu Arg Asp Ile Leu Val Glu Ala  
130 135 140

Asp Ser Leu Trp Val Val Lys Met Phe Tyr Ser Phe Gln Asp Lys Leu  
145 150 155 160

Asn Leu Tyr Leu Ile Met Glu Phe Leu Pro Gly Gly Asp Met Met Thr  
165 170 175

Leu Leu Met Lys Lys Asp Thr Leu Thr Glu Glu Glu Thr Gln Phe Tyr  
180 185 190

Ile Ala Glu Thr Val Leu Ala Ile Asp Ser Ile His Gln Leu Gly Phe  
195 200 205

Ile His Arg Asp Ile Lys Pro Asp Asn Leu Leu Leu Asp Ser Lys Gly  
210 215 220

His Val Lys Leu Ser Asp Phe Gly Leu Cys Thr Gly Leu Lys Lys Ala  
225 230 235 240

His Arg Thr Glu Phe Tyr Arg Asn Leu Asn His Ser Leu Pro Ser Asp  
 245 250 255  
 Phe Thr Phe Gln Asn Met Asn Ser Lys Arg Lys Ala Glu Thr Trp Lys  
 260 265 270  
 Arg Asn Arg Arg Gln Leu Ala Phe Ser Thr Val Gly Thr Pro Asp Tyr  
 275 280 285  
 Ile Ala Pro Glu Val Phe Met Gln Thr Gly Tyr Asn Lys Leu Cys Asp  
 290 295 300  
 Trp Trp Ser Leu Gly Val Ile Met Tyr Glu Met Leu Ile Gly Tyr Pro  
 305 310 315 320  
 Pro Phe Cys Ser Glu Thr Pro Gln Glu Thr Tyr Lys Lys Val Met Asn  
 325 330 335  
 Trp Lys Glu Thr Leu Thr Phe Pro Pro Glu Val Pro Ile Ser Glu Lys  
 340 345 350  
 Ala Lys Asp Leu Ile Leu Arg Phe Cys Cys Glu Trp Glu His Arg Ile  
 355 360 365  
 Gly Ala Pro Gly Val Glu Glu Ile Lys Ser Asn Ser Phe Phe Glu Gly  
 370 375 380  
 Val Asp Trp Glu His Ile Arg Glu Arg Pro Ala Ala Ile Ser Ile Glu  
 385 390 395 400  
 Ile Lys Ser Ile Asp Asp Thr Ser Asn Phe Asp Glu Phe Pro Glu Ser  
 405 410 415  
 Asp Ile Leu Lys Pro Thr Val Ala Thr Ser Asn His Pro Glu Thr Asp  
 420 425 430  
 Tyr Lys Asn Lys Asp Trp Val Phe Ile Asn Tyr Thr Tyr Lys Arg Phe  
 435 440 445  
 Glu Gly Leu Thr Ala Arg Gly Ala Ile Pro Ser Tyr Met Lys Ala Ala  
 450 455 460

Lys  
 465

<210> 192  
 <211> 73  
 <212> PRT  
 <213> Homo sapiens

<400> 192

Met Thr Tyr Phe Pro Leu Gly Arg Tyr Pro Val Val Gly Leu Leu Asp  
 1 5 10 15  
 Gln Met Val Val Leu Ser Thr Phe Ser Ser Leu Lys Asn Leu His Ile  
 20 25 30  
 Val Phe His Ser Gly Cys Thr Ser Leu His Ser His Gln Leu Cys Lys  
 35 40 45

Arg Val Pro Phe Ser Pro His Pro Arg Gln His Leu Leu Phe Phe Asp  
 50 55 60

Phe Trp Ile Lys Ala Ile Leu Ala Glu  
 65 70

<210> 193  
 <211> 410  
 <212> PRT  
 <213> Homo sapiens

<400> 193

Met Val Cys Phe Arg Leu Phe Pro Val Pro Gly Ser Gly Leu Val Leu  
 1 5 10 15

Val Cys Leu Val Leu Gly Ala Val Arg Ser Tyr Ala Leu Glu Leu Asn  
 20 25 30

Leu Thr Asp Ser Glu Asn Ala Thr Cys Leu Tyr Ala Lys Trp Gln Met  
 35 40 45

Asn Phe Thr Val Arg Tyr Glu Thr Thr Asn Lys Thr Tyr Lys Thr Val  
 50 55 60

Thr Ile Ser Asp His Gly Thr Val Thr Tyr Asn Gly Ser Ile Cys Gly  
 65 70 75 80

Asp Asp Gln Asn Gly Pro Lys Ile Ala Val Gln Phe Gly Pro Gly Phe  
 85 90 95

Ser Trp Ile Ala Asn Phe Thr Lys Ala Ala Ser Thr Tyr Ser Ile Asp  
 100 105 110

Ser Val Ser Phe Ser Tyr Asn Thr Gly Asp Asn Thr Thr Phe Pro Asp  
 115 120 125

Ala Glu Asp Lys Gly Ile Leu Thr Val Asp Glu Leu Leu Ala Ile Arg  
 130 135 140

Ile Pro Leu Asn Asp Leu Phe Arg Cys Asn Ser Leu Ser Thr Leu Glu  
 145 150 155 160

Lys Asn Asp Val Val Gln His Tyr Trp Asp Val Leu Val Gln Ala Phe  
 165 170 175

Val Gln Asn Gly Thr Val Ser Thr Asn Glu Phe Leu Cys Asp Lys Asp  
 180 185 190

Lys Thr Ser Thr Val Ala Pro Thr Ile His Thr Thr Val Pro Ser Pro  
 195 200 205

Thr Thr Thr Pro Thr Pro Lys Glu Lys Pro Glu Ala Gly Thr Tyr Ser  
 210 215 220

Val Asn Asn Gly Asn Asp Thr Cys Leu Leu Ala Thr Met Gly Leu Gln  
 225 230 235 240

Leu Asn Ile Thr Gln Asp Lys Val Ala Ser Val Ile Asn Ile Asn Pro  
 245 250 255

Asn Thr Thr His Ser Thr Gly Ser Cys Arg Ser His Thr Ala Leu Leu  
260 265 270

Arg Leu Asn Ser Ser Thr Ile Lys Tyr Leu Asp Phe Val Phe Ala Val  
275 280 285

Lys Asn Glu Asn Arg Phe Tyr Leu Lys Glu Val Asn Ile Ser Met Tyr  
290 295 300

Leu Val Asn Gly Ser Val Phe Ser Ile Ala Asn Asn Asn Leu Ser Tyr  
305 310 315 320

Trp Asp Ala Pro Leu Gly Ser Ser Tyr Met Cys Asn Lys Glu Gln Thr  
325 330 335

Val Ser Val Ser Gly Ala Phe Gln Ile Asn Thr Phe Asp Leu Arg Val  
340 345 350

Gln Pro Phe Asn Val Thr Gln Gly Lys Tyr Ser Thr Ala Gln Glu Cys  
355 360 365

Ser Leu Asp Asp Asp Thr Ile Leu Ile Pro Ile Ile Val Gly Ala Gly  
370 375 380

Leu Ser Gly Leu Ile Ile Val Ile Val Ile Ala Tyr Val Ile Gly Arg  
385 390 395 400

Arg Lys Ser Tyr Ala Gly Tyr Gln Thr Leu  
405 410

<210> 194

<211> 480

<212> PRT

<213> Homo sapiens

<400> 194

Met Ala Gly Gly Gly Gly Asp Leu Ser Thr Arg Arg Leu Asn Glu Cys  
1 5 10 15

Ile Ser Pro Val Ala Asn Glu Met Asn His Leu Pro Ala His Ser His  
20 25 30

Asp Leu Gln Arg Met Phe Thr Glu Asp Gln Gly Val Asp Asp Arg Leu  
35 40 45

Leu Tyr Asp Ile Val Phe Lys His Phe Lys Arg Asn Lys Val Glu Ile  
50 55 60

Ser Asn Ala Ile Lys Lys Thr Phe Pro Phe Leu Glu Gly Leu Arg Asp  
65 70 75 80

Arg Asp Leu Ile Thr Asn Lys Met Phe Glu Asp Ser Gln Asp Ser Cys  
85 90 95

Arg Asn Leu Val Pro Val Gln Arg Val Val Tyr Asn Val Leu Ser Glu  
100 105 110

Leu Glu Lys Thr Phe Asn Leu Pro Val Leu Glu Ala Leu Phe Ser Asp  
115 120 125

Val Asn Met Gln Glu Tyr Pro Asp Leu Ile His Ile Tyr Lys Gly Phe  
 130 135 140  
 Glu Asn Val Ile His Asp Lys Leu Pro Leu Gln Glu Ser Glu Glu Glu  
 145 150 155 160  
 Glu Arg Glu Glu Arg Ser Gly Leu Gln Leu Ser Leu Glu Gln Gly Thr  
 165 170 175  
 Gly Glu Asn Ser Phe Arg Ser Leu Thr Trp Pro Pro Ser Gly Ser Pro  
 180 185 190  
 Ser His Ala Gly Thr Thr Pro Pro Glu Asn Gly Leu Ser Glu His Pro  
 195 200 205  
 Cys Glu Thr Glu Gln Ile Asn Ala Lys Arg Lys Asp Thr Thr Ser Asp  
 210 215 220  
 Lys Asp Asp Ser Leu Gly Ser Gln Gln Thr Asn Glu Gln Cys Ala Gln  
 225 230 235 240  
 Lys Ala Glu Pro Thr Glu Ser Cys Glu Gln Ile Ala Val Gln Val Asn  
 245 250 255  
 Asn Gly Asp Ala Gly Arg Glu Met Pro Cys Pro Leu Pro Cys Asp Glu  
 260 265 270  
 Glu Ser Pro Glu Ala Glu Leu His Asn His Gly Ile Gln Ile Asn Ser  
 275 280 285  
 Cys Ser Val Arg Leu Val Asp Ile Lys Lys Glu Lys Pro Phe Ser Asn  
 290 295 300  
 Ser Lys Val Glu Cys Gln Ala Gln Ala Arg Thr His His Asn Gln Ala  
 305 310 315 320  
 Ser Asp Ile Ile Val Ile Ser Ser Glu Asp Ser Glu Gly Ser Thr Asp  
 325 330 335  
 Val Asp Glu Pro Leu Glu Val Phe Ile Ser Ala Pro Arg Ser Glu Pro  
 340 345 350  
 Val Ile Asn Asn Asp Asn Pro Leu Glu Ser Asn Asp Glu Lys Glu Gly  
 355 360 365  
 Gln Glu Ala Thr Cys Ser Arg Pro Gln Ile Val Pro Glu Pro Met Asp  
 370 375 380  
 Phe Arg Lys Leu Ser Thr Phe Arg Glu Ser Phe Lys Lys Arg Val Ile  
 385 390 395 400  
 Gly Gln Asp His Asp Phe Ser Glu Ser Ser Glu Glu Glu Ala Pro Ala  
 405 410 415  
 Glu Ala Ser Ser Gly Ala Leu Arg Ser Lys His Gly Glu Lys Ala Pro  
 420 425 430  
 Met Thr Ser Arg Ser Thr Ser Thr Trp Arg Ile Pro Ser Arg Lys Arg  
 435 440 445



Arg Phe Ser Ser Ser Asp Phe Ser Asp Leu Ser Asn Gly Glu Glu Leu  
450 455 460

Gln Glu Thr Cys Ser Ser Ser Leu Arg Arg Gly Ser Gly Lys Glu Asp  
465 470 475 480

<210> 195  
<211> 339  
<212> PRT  
<213> Homo sapiens

<400> 195

Met Trp Gln Leu Trp Ala Ser Leu Cys Cys Leu Leu Val Leu Ala Asn  
1 5 10 15

Ala Arg Ser Arg Pro Ser Phe His Pro Leu Ser Asp Glu Leu Val Asn  
20 25 30

Tyr Val Asn Lys Arg Asn Thr Thr Trp Gln Ala Gly His Asn Phe Tyr  
35 40 45

Asn Val Asp Met Ser Tyr Leu Lys Arg Leu Cys Gly Thr Phe Leu Gly  
50 55 60

Gly Pro Lys Pro Pro Gln Arg Val Met Phe Thr Glu Asp Leu Lys Leu  
65 70 75 80

Pro Ala Ser Phe Asp Ala Arg Glu Gln Trp Pro Gln Cys Pro Thr Ile  
85 90 95

Lys Glu Ile Arg Asp Gln Gly Ser Cys Gly Ser Cys Trp Ala Phe Gly  
100 105 110

Ala Val Glu Ala Ile Ser Asp Arg Ile Cys Ile His Thr Asn Ala His  
115 120 125

Val Ser Val Glu Val Ser Ala Glu Asp Leu Leu Thr Cys Cys Gly Ser  
130 135 140

Met Cys Gly Asp Gly Cys Asn Gly Gly Tyr Pro Ala Glu Ala Trp Asn  
145 150 155 160

Phe Trp Thr Arg Lys Gly Leu Val Ser Gly Gly Leu Tyr Glu Ser His  
165 170 175

Val Gly Cys Arg Pro Tyr Ser Ile Pro Pro Cys Glu His His Val Asn  
180 185 190

Gly Ser Arg Pro Pro Cys Thr Gly Glu Gly Asp Thr Pro Lys Cys Ser  
195 200 205

Lys Ile Cys Glu Pro Gly Tyr Ser Pro Thr Tyr Lys Gln Asp Lys His  
210 215 220

Tyr Gly Tyr Asn Ser Tyr Ser Val Ser Asn Ser Glu Lys Asp Ile Met  
225 230 235 240

Ala Glu Ile Tyr Lys Asn Gly Pro Val Glu Gly Ala Phe Ser Val Tyr  
245 250 255

Ser Asp Phe Leu Leu Tyr Lys Ser Gly Val Tyr Gln His Val Thr Gly  
260 265 270

Glu Met Met Gly Gly His Ala Ile Arg Ile Leu Gly Trp Gly Val Glu  
275 280 285

Asn Gly Thr Pro Tyr Trp Leu Val Ala Asn Ser Trp Asn Thr Asp Trp  
290 295 300

Gly Asp Asn Gly Phe Phe Lys Ile Leu Arg Gly Gln Asp His Cys Gly  
305 310 315 320

Ile Glu Ser Glu Val Val Ala Gly Ile Pro Arg Thr Asp Gln Tyr Trp  
325 330 335

Glu Lys Ile

<210> 196  
<211> 2328  
<212> PRT  
<213> Homo sapiens

<400> 196

Lys Ser Lys Arg Gln Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val  
1 5 10 15

Ala Val Ser Gln Ser Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr  
20 25 30

Gln Ile Asn Gln Gln Trp Glu Arg Thr Tyr Leu Gly Asn Val Leu Val  
35 40 45

Cys Thr Cys Tyr Gly Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro  
50 55 60

Glu Ala Glu Glu Thr Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg  
65 70 75 80

Val Gly Asp Thr Tyr Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys  
85 90 95

Thr Cys Ile Gly Ala Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn  
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Val Tyr Ser Pro Ser Val Glu Gly Ser Ser Thr Glu Leu Asn Leu Pro  
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Pro Pro 1790	Arg Arg Ala Arg Val 1795	Thr Asp Ala Thr Glu Thr Thr Ile 1800
Thr Ile 1805	Ser Trp Arg Thr Lys 1810	Thr Glu Thr Ile Thr Gly Phe Gln 1815
Val Asp 1820	Ala Val Pro Ala Asn 1825	Gly Gln Thr Pro Ile Gln Arg Thr 1830
Ile Lys 1835	Pro Asp Val Arg Ser 1840	Tyr Thr Ile Thr Gly Leu Gln Pro 1845
Gly Thr 1850	Asp Tyr Lys Ile Tyr 1855	Leu Tyr Thr Leu Asn Asp Asn Ala 1860
Arg Ser 1865	Ser Pro Val Val Ile 1870	Asp Ala Ser Thr Ala Ile Asp Ala 1875
Pro Ser 1880	Asn Leu Arg Phe Leu 1885	Ala Thr Thr Pro Asn Ser Leu Leu 1890
Val Ser 1895	Trp Gln Pro Pro Arg 1900	Ala Arg Ile Thr Gly Tyr Ile Ile 1905
Lys Tyr 1910	Glu Lys Pro Gly Ser 1915	Pro Pro Arg Glu Val Val Pro Arg 1920
Pro Arg 1925	Pro Gly Val Thr Glu 1930	Ala Thr Ile Thr Gly Leu Glu Pro 1935
Gly Thr 1940	Glu Tyr Thr Ile Tyr 1945	Val Ile Ala Leu Lys Asn Asn Gln 1950
Lys Ser 1955	Glu Pro Leu Ile Gly 1960	Arg Lys Lys Thr Asp Glu Leu Pro 1965
Gln Leu 1970	Val Thr Leu Pro His 1975	Pro Asn Leu His Gly Pro Glu Ile 1980
Leu Asp 1985	Val Pro Ser Thr Val 1990	Gln Lys Thr Pro Phe Val Thr His 1995
Pro Gly 2000	Tyr Asp Thr Gly Asn 2005	Gly Ile Gln Leu Pro Gly Thr Ser 2010



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Ser Arg Pro Glu Thr Gly Arg Pro Arg Pro Lys Gly Leu Glu Gly Glu  
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Arg Ser Ala Val Pro Pro Gly Ala Asp Lys Lys Ala Glu Ala Gly Ala  
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Gly Gln Pro Pro Gln  
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His Glu Phe Gly Asp Asn Thr Ala Gly Cys Thr Ser Ala Gly Pro His  
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Phe Asn Pro Leu Ser Arg Lys His Gly Gly Pro Lys Asp Glu Glu Arg  
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Gln Gly Thr Thr Asn Val His Ser Ser Glu His Ala Gly Arg Asn Gly  
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Pro Val Leu Lys Lys Ile Ile Lys Glu Gln Pro Gln Pro Ser Gly Lys  
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Asp Gln Arg Arg Arg Ser Cys Lys Thr Ala Pro Ala Ser Ser Ser Lys  
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 Pro Gln Pro Asp Pro Val Lys Thr Pro Thr Ser Ser Lys Gln Arg  
 1985 1990 1995  
 Leu Lys Ile Ser Leu Gly Lys Val Gly Val Lys Glu Glu Val Leu  
 2000 2005 2010  
 Pro Val Gly Lys Leu Thr Gln Thr Ser Gly Lys Thr Thr Gln Thr  
 2015 2020 2025

His Arg Glu Thr Ala Gly Asp Gly Lys Ser Ile Lys Ala Phe Lys  
 2030 2035 2040  
 Glu Ser Ala Lys Gln Met Leu Asp Pro Ala Asn Tyr Gly Thr Gly  
 2045 2050 2055  
 Met Glu Arg Trp Pro Arg Thr Pro Lys Glu Glu Ala Gln Ser Leu  
 2060 2065 2070  
 Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Asp His  
 2075 2080 2085  
 Thr Glu Glu Ser Thr Thr Asp Asp Lys Thr Thr Lys Ile Ala Cys  
 2090 2095 2100  
 Lys Ser Pro Pro Pro Glu Ser Met Asp Thr Pro Thr Ser Thr Arg  
 2105 2110 2115  
 Arg Arg Pro Lys Thr Pro Leu Gly Lys Arg Asp Ile Val Glu Glu  
 2120 2125 2130  
 Leu Ser Ala Leu Lys Gln Leu Thr Gln Thr Thr His Thr Asp Lys  
 2135 2140 2145  
 Val Pro Gly Asp Glu Asp Lys Gly Ile Asn Val Phe Arg Glu Thr  
 2150 2155 2160  
 Ala Lys Gln Lys Leu Asp Pro Ala Ala Ser Val Thr Gly Ser Lys  
 2165 2170 2175  
 Arg Gln Pro Arg Thr Pro Lys Gly Lys Ala Gln Pro Leu Glu Asp  
 2180 2185 2190  
 Leu Ala Gly Leu Lys Glu Leu Phe Gln Thr Pro Val Cys Thr Asp  
 2195 2200 2205  
 Lys Pro Thr Thr His Glu Lys Thr Thr Lys Ile Ala Cys Arg Ser  
 2210 2215 2220  
 Pro Gln Pro Asp Pro Val Gly Thr Pro Thr Ile Phe Lys Pro Gln  
 2225 2230 2235  
 Ser Lys Arg Ser Leu Arg Lys Ala Asp Val Glu Glu Glu Ser Leu  
 2240 2245 2250  
 Ala Leu Arg Lys Arg Thr Pro Ser Val Gly Lys Ala Met Asp Thr  
 2255 2260 2265  
 Pro Lys Pro Ala Gly Gly Asp Glu Lys Asp Met Lys Ala Phe Met  
 2270 2275 2280  
 Gly Thr Pro Val Gln Lys Leu Asp Leu Pro Gly Asn Leu Pro Gly  
 2285 2290 2295  
 Ser Lys Arg Trp Pro Gln Thr Pro Lys Glu Lys Ala Gln Ala Leu  
 2300 2305 2310  
 Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly Thr

2315	2320	2325
Asp Lys Pro Thr Thr Asp Glu Lys Thr Thr Lys Ile Ala Cys Lys 2330 2335 2340		
Ser Pro Gln Pro Asp Pro Val Asp Thr Pro Ala Ser Thr Lys Gln 2345 2350 2355		
Arg Pro Lys Arg Asn Leu Arg Lys Ala Asp Val Glu Glu Glu Phe 2360 2365 2370		
Leu Ala Leu Arg Lys Arg Thr Pro Ser Ala Gly Lys Ala Met Asp 2375 2380 2385		
Thr Pro Lys Pro Ala Val Ser Asp Glu Lys Asn Ile Asn Thr Phe 2390 2395 2400		
Val Glu Thr Pro Val Gln Lys Leu Asp Leu Leu Gly Asn Leu Pro 2405 2410 2415		
Gly Ser Lys Arg Gln Pro Gln Thr Pro Lys Glu Lys Ala Glu Ala 2420 2425 2430		
Leu Glu Asp Leu Val Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly 2435 2440 2445		
His Thr Glu Glu Ser Met Thr Asp Asp Lys Ile Thr Glu Val Ser 2450 2455 2460		
Cys Lys Ser Pro Gln Pro Glu Ser Phe Lys Thr Ser Arg Ser Ser 2465 2470 2475		
Lys Gln Arg Leu Lys Ile Pro Leu Val Lys Val Asp Met Lys Glu 2480 2485 2490		
Glu Pro Leu Ala Val Ser Lys Leu Thr Arg Thr Ser Gly Glu Thr 2495 2500 2505		
Thr Gln Thr His Thr Glu Pro Thr Gly Asp Ser Lys Ser Ile Lys 2510 2515 2520		
Ala Phe Lys Glu Ser Pro Lys Gln Ile Leu Asp Pro Ala Ala Ser 2525 2530 2535		
Val Thr Gly Ser Arg Arg Gln Leu Arg Thr Arg Lys Glu Lys Ala 2540 2545 2550		
Arg Ala Leu Glu Asp Leu Val Asp Phe Lys Glu Leu Phe Ser Ala 2555 2560 2565		
Pro Gly His Thr Glu Glu Ser Met Thr Ile Asp Lys Asn Thr Lys 2570 2575 2580		
Ile Pro Cys Lys Ser Pro Pro Pro Glu Leu Thr Asp Thr Ala Thr 2585 2590 2595		
Ser Thr Lys Arg Cys Pro Lys Thr Arg Pro Arg Lys Glu Val Lys 2600 2605 2610		

Glu Glu Leu Ser Ala Val Glu Arg Leu Thr Gln Thr Ser Gly Gln  
 2615 2620 2625  
 Ser Thr His Thr His Lys Glu Pro Ala Ser Gly Asp Glu Gly Ile  
 2630 2635 2640  
 Lys Val Leu Lys Gln Arg Ala Lys Lys Lys Pro Asn Pro Val Glu  
 2645 2650 2655  
 Glu Glu Pro Ser Arg Arg Arg Pro Arg Ala Pro Lys Glu Lys Ala  
 2660 2665 2670  
 Gln Pro Leu Glu Asp Leu Ala Gly Phe Thr Glu Leu Ser Glu Thr  
 2675 2680 2685  
 Ser Gly His Thr Gln Glu Ser Leu Thr Ala Gly Lys Ala Thr Lys  
 2690 2695 2700  
 Ile Pro Cys Glu Ser Pro Pro Leu Glu Val Val Asp Thr Thr Ala  
 2705 2710 2715  
 Ser Thr Lys Arg His Leu Arg Thr Arg Val Gln Lys Val Gln Val  
 2720 2725 2730  
 Lys Glu Glu Pro Ser Ala Val Lys Phe Thr Gln Thr Ser Gly Glu  
 2735 2740 2745  
 Thr Thr Asp Ala Asp Lys Glu Pro Ala Gly Glu Asp Lys Gly Ile  
 2750 2755 2760  
 Lys Ala Leu Lys Glu Ser Ala Lys Gln Thr Pro Ala Pro Ala Ala  
 2765 2770 2775  
 Ser Val Thr Gly Ser Arg Arg Arg Pro Arg Ala Pro Arg Glu Ser  
 2780 2785 2790  
 Ala Gln Ala Ile Glu Asp Leu Ala Gly Phe Lys Asp Pro Ala Ala  
 2795 2800 2805  
 Gly His Thr Glu Glu Ser Met Thr Asp Asp Lys Thr Thr Lys Ile  
 2810 2815 2820  
 Pro Cys Lys Ser Ser Pro Glu Leu Glu Asp Thr Ala Thr Ser Ser  
 2825 2830 2835  
 Lys Arg Arg Pro Arg Thr Arg Ala Gln Lys Val Glu Val Lys Glu  
 2840 2845 2850  
 Glu Leu Leu Ala Val Gly Lys Leu Thr Gln Thr Ser Gly Glu Thr  
 2855 2860 2865  
 Thr His Thr Asp Lys Glu Pro Val Gly Glu Gly Lys Gly Thr Lys  
 2870 2875 2880  
 Ala Phe Lys Gln Pro Ala Lys Arg Asn Val Asp Ala Glu Asp Val  
 2885 2890 2895  
 Ile Gly Ser Arg Arg Gln Pro Arg Ala Pro Lys Glu Lys Ala Gln  
 2900 2905 2910

Pro Leu Glu Asp Leu Ala Ser Phe Gln Glu Leu Ser Gln Thr Pro  
 2915 2920 2925  
 Gly His Thr Glu Glu Leu Ala Asn Gly Ala Ala Asp Ser Phe Thr  
 2930 2935 2940  
 Ser Ala Pro Lys Gln Thr Pro Asp Ser Gly Lys Pro Leu Lys Ile  
 2945 2950 2955  
 Ser Arg Arg Val Leu Arg Ala Pro Lys Val Glu Pro Val Gly Asp  
 2960 2965 2970  
 Val Val Ser Thr Arg Asp Pro Val Lys Ser Gln Ser Lys Ser Asn  
 2975 2980 2985  
 Thr Ser Leu Pro Pro Leu Pro Phe Lys Arg Gly Gly Gly Lys Asp  
 2990 2995 3000  
 Gly Ser Val Thr Gly Thr Lys Arg Leu Arg Cys Met Pro Ala Pro  
 3005 3010 3015  
 Glu Glu Ile Val Glu Glu Leu Pro Ala Ser Lys Lys Gln Arg Val  
 3020 3025 3030  
 Ala Pro Arg Ala Arg Gly Lys Ser Ser Glu Pro Val Val Ile Met  
 3035 3040 3045  
 Lys Arg Ser Leu Arg Thr Ser Ala Lys Arg Ile Glu Pro Ala Glu  
 3050 3055 3060  
 Glu Leu Asn Ser Asn Asp Met Lys Thr Asn Lys Glu Glu His Lys  
 3065 3070 3075  
 Leu Gln Asp Ser Val Pro Glu Asn Lys Gly Ile Ser Leu Arg Ser  
 3080 3085 3090  
 Arg Arg Gln Asp Lys Thr Glu Ala Glu Gln Gln Ile Thr Glu Val  
 3095 3100 3105  
 Phe Val Leu Ala Glu Arg Ile Glu Ile Asn Arg Asn Glu Lys Lys  
 3110 3115 3120  
 Pro Met Lys Thr Ser Pro Glu Met Asp Ile Gln Asn Pro Asp Asp  
 3125 3130 3135  
 Gly Ala Arg Lys Pro Ile Pro Arg Asp Lys Val Thr Glu Asn Lys  
 3140 3145 3150  
 Arg Cys Leu Arg Ser Ala Arg Gln Asn Glu Ser Ser Gln Pro Lys  
 3155 3160 3165  
 Val Ala Glu Glu Ser Gly Gly Gln Lys Ser Ala Lys Val Leu Met  
 3170 3175 3180  
 Gln Asn Gln Lys Gly Lys Gly Glu Ala Gly Asn Ser Asp Ser Met  
 3185 3190 3195  
 Cys Leu Arg Ser Arg Lys Thr Lys Ser Gln Pro Ala Ala Ser Thr  
 3200 3205 3210

Leu Glu Ser Lys Ser Val Gln Arg Val Thr Arg Ser Val Lys Arg  
 3215 3220 3225

Cys Ala Glu Asn Pro Lys Lys Ala Glu Asp Asn Val Cys Val Lys  
 3230 3235 3240

Lys Ile Thr Thr Arg Ser His Arg Asp Ser Glu Asp Ile  
 3245 3250 3255

<210> 200  
 <211> 478  
 <212> PRT  
 <213> Homo sapiens

<400> 200

Met Ala Gly Val Glu Glu Val Ala Ala Ser Gly Ser His Leu Asn Gly  
 1 5 10 15

Asp Leu Asp Pro Asp Asp Arg Glu Glu Gly Ala Ala Ser Thr Ala Glu  
 20 25 30

Glu Ala Ala Lys Lys Lys Arg Arg Lys Lys Lys Lys Ser Lys Gly Pro  
 35 40 45

Ser Ala Ala Gly Glu Gln Glu Pro Asp Lys Glu Ser Gly Ala Ser Val  
 50 55 60

Asp Glu Val Ala Arg Gln Leu Glu Arg Ser Ala Leu Glu Asp Lys Glu  
 65 70 75 80

Arg Asp Glu Asp Asp Glu Asp Gly Asp Gly Asp Gly Asp Gly Ala Thr  
 85 90 95

Gly Lys Lys Lys Lys Lys Lys Lys Lys Arg Gly Pro Lys Val Gln  
 100 105 110

Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val  
 115 120 125

Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg  
 130 135 140

Thr Ala Ala Trp Arg Thr Thr Ser Glu Glu Lys Lys Ala Leu Asp Gln  
 145 150 155 160

Ala Ser Glu Glu Ile Trp Asn Asp Phe Arg Glu Ala Ala Glu Ala His  
 165 170 175

Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr  
 180 185 190

Met Ile Glu Ile Cys Glu Lys Leu Glu Asp Cys Ser Arg Lys Leu Ile  
 195 200 205

Lys Glu Asn Gly Leu Asn Ala Gly Leu Ala Phe Pro Thr Gly Cys Ser  
 210 215 220

Leu Asn Asn Cys Ala Ala His Tyr Thr Pro Asn Ala Gly Asp Thr Thr  
 225 230 235 240

Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Asp Phe Gly Thr His Ile  
245 250 255

Ser Gly Arg Ile Ile Asp Cys Ala Phe Thr Val Thr Phe Asn Pro Lys  
260 265 270

Tyr Asp Thr Leu Leu Lys Ala Val Lys Asp Ala Thr Asn Thr Gly Ile  
275 280 285

Lys Cys Ala Gly Ile Asp Val Arg Leu Cys Asp Val Gly Glu Ala Ile  
290 295 300

Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr  
305 310 315 320

Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Gln Tyr  
325 330 335

Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala  
340 345 350

Thr Arg Met Glu Glu Gly Glu Val Tyr Ala Ile Glu Thr Phe Gly Ser  
355 360 365

Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met  
370 375 380

Lys Asn Phe Asp Val Gly His Val Pro Ile Arg Leu Pro Arg Thr Lys  
385 390 395 400

His Leu Leu Asn Val Ile Asn Glu Asn Phe Gly Thr Leu Ala Phe Cys  
405 410 415

Arg Arg Trp Leu Asp Arg Leu Gly Glu Ser Lys Tyr Leu Met Ala Leu  
420 425 430

Lys Asn Leu Cys Asp Leu Gly Ile Val Asp Pro Tyr Pro Pro Leu Cys  
435 440 445

Asp Ile Lys Gly Ser Tyr Thr Ala Gln Phe Glu His Thr Ile Leu Leu  
450 455 460

Arg Pro Thr Cys Lys Glu Val Val Ser Arg Gly Asp Asp Tyr  
465 470 475

<210> 201  
<211> 488  
<212> PRT  
<213> Homo sapiens

<400> 201

Met His Gly Arg Lys Asp Asp Ala Gln Lys Gln Pro Val Lys Asn Gln  
1 5 10 15

Leu Gly Leu Asn Pro Gln Ser His Leu Pro Glu Leu Gln Leu Phe Gln  
20 25 30

Ala Glu Gly Lys Ile Tyr Lys Tyr Asp His Met Glu Lys Ser Val Asn  
35 40 45

Ser Ser Ser Leu Val Ser Pro Pro Gln Arg Ile Ser Ser Thr Val Lys  
 50 55 60  
 Thr His Ile Ser His Ile Tyr Glu Cys Asn Phe Val Asp Ser Leu Phe  
 65 70 75 80  
 Thr Gln Lys Glu Lys Ala Asn Ile Gly Thr Glu His Tyr Lys Cys Asn  
 85 90 95  
 Glu Arg Gly Lys Ala Phe His Gln Gly Leu His Phe Thr Ile His Gln  
 100 105 110  
 Ile Ile His Thr Lys Glu Thr Gln Phe Lys Cys Asp Ile Cys Gly Lys  
 115 120 125  
 Ile Phe Asn Lys Lys Ser Asn Leu Ala Ser His Gln Arg Ile His Thr  
 130 135 140  
 Gly Glu Lys Pro Tyr Lys Cys Asn Glu Cys Gly Lys Val Phe His Asn  
 145 150 155 160  
 Met Ser His Leu Ala Gln His Arg Arg Ile His Thr Gly Glu Lys Pro  
 165 170 175  
 Tyr Lys Cys Asn Glu Cys Gly Lys Val Phe Asn Gln Ile Ser His Leu  
 180 185 190  
 Ala Gln His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys Asn  
 195 200 205  
 Glu Cys Gly Lys Val Phe His Gln Ile Ser His Leu Ala Gln His Arg  
 210 215 220  
 Thr Ile His Thr Gly Glu Lys Pro Tyr Glu Cys Asn Lys Cys Gly Lys  
 225 230 235 240  
 Val Phe Ser Arg Asn Ser Tyr Leu Val Gln His Leu Ile Ile His Thr  
 245 250 255  
 Gly Glu Lys Pro Tyr Arg Cys Asn Val Cys Gly Lys Val Phe Ser His  
 260 265 270  
 Lys Ser Ser Leu Val Asn His Trp Arg Ile His Thr Gly Glu Lys Pro  
 275 280 285  
 Tyr Lys Cys Asn Glu Cys Gly Lys Val Phe Ser His Lys Ser Ser Leu  
 290 295 300  
 Val Asn His Trp Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys Asn  
 305 310 315 320  
 Glu Cys Gly Lys Val Phe Ser Arg Asn Ser Tyr Leu Ala Gln His Leu  
 325 330 335  
 Ile Ile His Ala Gly Glu Lys Pro Tyr Lys Cys Asp Glu Cys Asp Lys  
 340 345 350  
 Ala Phe Ser Gln Asn Ser His Leu Val Gln His His Arg Ile His Thr



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355          360          365
Gly Glu Lys Pro Tyr Lys Cys Asp Glu Cys Gly Lys Val Phe Ser Gln
370          375          380
Asn Ser Tyr Leu Ala Tyr His Trp Arg Ile His Thr Gly Glu Lys Ala
385          390          395          400
Tyr Lys Cys Asn Glu Cys Gly Lys Val Phe Gly Leu Asn Ser Ser Leu
405          410          415
Ala His His Arg Lys Ile His Thr Gly Glu Lys Pro Phe Lys Cys Asn
420          425          430
Glu Cys Gly Lys Ala Phe Ser Met Arg Ser Ser Leu Thr Asn His His
435          440          445
Ala Ile His Thr Gly Glu Lys His Phe Lys Cys Asn Glu Cys Gly Lys
450          455          460
Leu Phe Arg Asp Asn Ser Tyr Leu Val Arg His Gln Arg Phe His Ala
465          470          475          480
Gly Lys Lys Ser Asn Thr Cys Asn
485

<210> 202
<211> 553
<212> PRT
<213> Homo sapiens

<400> 202
Met Leu Ser Val Arg Val Ala Ala Ala Val Val Arg Ala Leu Pro Arg
1          5          10          15
Arg Ala Gly Leu Val Ser Arg Asn Ala Leu Gly Ser Ser Phe Ile Ala
20          25          30
Ala Arg Asn Phe His Ala Ser Asn Thr His Leu Gln Lys Thr Gly Thr
35          40          45
Ala Glu Met Ser Ser Ile Leu Glu Glu Arg Ile Leu Gly Ala Asp Thr
50          55          60
Ser Val Asp Leu Glu Glu Thr Gly Arg Val Leu Ser Ile Gly Asp Gly
65          70          75          80
Ile Ala Arg Val His Gly Leu Arg Asn Val Gln Ala Glu Glu Met Val
85          90          95
Glu Phe Ser Ser Gly Leu Lys Gly Met Ser Leu Asn Leu Glu Pro Asp
100         105         110
Asn Val Gly Val Val Val Phe Gly Asn Asp Lys Leu Ile Lys Glu Gly
115         120         125
Asp Ile Val Lys Arg Thr Gly Ala Ile Val Asp Val Pro Val Gly Glu
130         135         140
Glu Leu Leu Gly Arg Val Val Asp Ala Leu Gly Asn Ala Ile Asp Gly

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145                      150                      155                      160  
 Lys Gly Pro Ile Gly Ser Lys Thr Arg Arg Arg Val Gly Leu Lys Ala  
                                  165                                   170                                   175  
 Pro Gly Ile Ile Pro Arg Ile Ser Val Arg Glu Pro Met Gln Thr Gly  
                                  180                                   185                                   190  
 Ile Lys Ala Val Asp Ser Leu Val Pro Ile Gly Arg Gly Gln Arg Glu  
                                  195                                   200                                   205  
 Leu Ile Ile Gly Asp Arg Gln Thr Gly Lys Thr Ser Ile Ala Ile Asp  
                                  210                                   215                                   220  
 Thr Ile Ile Asn Gln Lys Arg Phe Asn Asp Gly Ser Asp Glu Lys Lys  
                                  225                                   230                                   235                                   240  
 Lys Leu Tyr Cys Ile Tyr Val Ala Ile Gly Gln Lys Arg Ser Thr Val  
                                  245                                   250                                   255  
 Ala Gln Leu Val Lys Arg Leu Thr Asp Ala Asp Ala Met Lys Tyr Thr  
                                  260                                   265                                   270  
 Ile Val Val Ser Ala Thr Ala Ser Asp Ala Ala Pro Leu Gln Tyr Leu  
                                  275                                   280                                   285  
 Ala Pro Tyr Ser Gly Cys Ser Met Gly Glu Tyr Phe Arg Asp Asn Gly  
                                  290                                   295                                   300  
 Lys His Ala Leu Ile Ile Tyr Asp Asp Leu Ser Lys Gln Ala Val Ala  
                                  305                                   310                                   315                                   320  
 Tyr Arg Gln Met Ser Leu Leu Leu Arg Arg Pro Pro Gly Arg Glu Ala  
                                  325                                   330                                   335  
 Tyr Pro Gly Asp Val Phe Tyr Leu His Ser Arg Leu Leu Glu Arg Ala  
                                  340                                   345                                   350  
 Ala Lys Met Asn Asp Ala Phe Gly Gly Gly Ser Leu Thr Ala Leu Pro  
                                  355                                   360                                   365  
 Val Ile Glu Thr Gln Ala Gly Asp Val Ser Ala Tyr Ile Pro Thr Asn  
                                  370                                   375                                   380  
 Val Ile Ser Ile Thr Asp Gly Gln Ile Phe Leu Glu Thr Glu Leu Phe  
                                  385                                   390                                   395                                   400  
 Tyr Lys Gly Ile Arg Pro Ala Ile Asn Val Gly Leu Ser Val Ser Arg  
                                  405                                   410                                   415  
 Val Gly Ser Ala Ala Gln Thr Arg Ala Met Lys Gln Val Ala Gly Thr  
                                  420                                   425                                   430  
 Met Lys Leu Glu Leu Ala Gln Tyr Arg Glu Val Ala Ala Phe Ala Gln  
                                  435                                   440                                   445  
 Phe Gly Ser Asp Leu Asp Ala Ala Thr Gln Gln Leu Leu Ser Arg Gly  
                                  450                                   455                                   460

Val Arg Leu Thr Glu Leu Leu Lys Gln Gly Gln Tyr Ser Pro Met Ala  
465 470 475 480

Ile Glu Glu Gln Val Ala Val Ile Tyr Ala Gly Val Arg Gly Tyr Leu  
485 490 495

Asp Lys Leu Glu Pro Ser Lys Ile Thr Lys Phe Glu Asn Ala Phe Leu  
500 505 510

Ser His Val Val Ser Gln His Gln Ala Leu Leu Gly Thr Ile Arg Ala  
515 520 525

Asp Gly Lys Ile Ser Glu Gln Ser Asp Ala Lys Leu Lys Glu Ile Val  
530 535 540

Thr Asn Phe Leu Ala Gly Phe Glu Ala  
545 550

<210> 203  
<211> 462  
<212> PRT  
<213> Homo sapiens

<400> 203

Met Gly Lys Glu Lys Thr His Ile Asn Ile Val Val Ile Gly His Val  
1 5 10 15

Asp Ser Gly Lys Ser Thr Thr Thr Gly His Leu Ile Tyr Lys Cys Gly  
20 25 30

Gly Ile Asp Lys Arg Thr Ile Glu Lys Phe Glu Lys Glu Ala Ala Glu  
35 40 45

Met Gly Lys Gly Ser Phe Lys Tyr Ala Trp Val Leu Asp Lys Leu Lys  
50 55 60

Ala Glu Arg Glu Arg Gly Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe  
65 70 75 80

Glu Thr Ser Lys Tyr Tyr Val Thr Ile Ile Asp Ala Pro Gly His Arg  
85 90 95

Asp Phe Ile Lys Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala  
100 105 110

Val Leu Ile Val Ala Ala Gly Val Gly Glu Phe Glu Ala Gly Ile Ser  
115 120 125

Lys Asn Gly Gln Thr Arg Glu His Ala Leu Leu Ala Tyr Thr Leu Gly  
130 135 140

Val Lys Gln Leu Ile Val Gly Val Asn Lys Met Asp Ser Thr Glu Pro  
145 150 155 160

Pro Tyr Ser Gln Lys Arg Tyr Glu Glu Ile Val Lys Glu Val Ser Thr  
165 170 175

Tyr Ile Lys Lys Ile Gly Tyr Asn Pro Asp Thr Val Ala Phe Val Pro  
180 185 190

Ile Ser Gly Trp Asn Gly Asp Asn Met Leu Glu Pro Ser Ala Asn Met  
195 200 205

Pro Trp Phe Lys Gly Trp Lys Val Thr Arg Lys Asp Gly Asn Ala Ser  
210 215 220

Gly Thr Thr Leu Leu Glu Ala Val Asp Cys Ile Leu Pro Pro Thr Arg  
225 230 235 240

Pro Thr Asp Lys Pro Leu Arg Leu Pro Leu Gln Asp Val Tyr Lys Ile  
245 250 255

Gly Gly Ile Gly Thr Val Pro Val Gly Arg Val Glu Thr Gly Val Leu  
260 265 270

Lys Pro Gly Met Val Val Thr Phe Ala Pro Val Asn Val Thr Thr Glu  
275 280 285

Val Lys Ser Val Glu Met His His Glu Ala Leu Ser Glu Ala Leu Pro  
290 295 300

Gly Asp Asn Val Gly Phe Asn Val Lys Asn Val Ser Val Lys Asp Val  
305 310 315 320

Arg Arg Gly Asn Val Ala Gly Asp Ser Lys Asn Asp Pro Pro Met Glu  
325 330 335

Ala Ala Gly Phe Thr Ala Gln Val Ile Ile Leu Asn His Pro Gly Gln  
340 345 350

Ile Ser Ala Gly Tyr Ala Pro Val Leu Asp Cys His Thr Ala His Ile  
355 360 365

Ala Cys Lys Phe Ala Glu Leu Lys Glu Lys Ile Asp Arg Arg Ser Gly  
370 375 380

Lys Lys Leu Glu Asp Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala  
385 390 395 400

Ile Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser  
405 410 415

Asp Tyr Pro Pro Leu Gly Arg Phe Ala Val Arg Asp Met Arg Gln Thr  
420 425 430

Val Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Ala Gly Ala  
435 440 445

Gly Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys  
450 455 460

<210> 204  
<211> 1069  
<212> PRT  
<213> Homo sapiens

<400> 204

Met Leu Arg Met Arg Thr Ala Gly Trp Ala Arg Gly Trp Cys Leu Gly  
1 5 10 15

Cys Cys Leu Leu Leu Pro Leu Ser Phe Ser Leu Ala Ala Ala Lys Gln  
 20 25 30  
 Leu Leu Arg Tyr Arg Leu Ala Glu Glu Gly Pro Ala Asp Val Arg Ile  
 35 40 45  
 Gly Asn Val Ala Ser Asp Leu Gly Ile Val Thr Gly Ser Gly Glu Val  
 50 55 60  
 Thr Phe Ser Leu Glu Ser Gly Ser Glu Tyr Leu Lys Ile Asp Asn Leu  
 65 70 75 80  
 Thr Gly Glu Leu Ser Thr Ser Glu Arg Arg Ile Asp Arg Glu Lys Leu  
 85 90 95  
 Pro Gln Cys Gln Met Ile Phe Asp Glu Asn Glu Cys Phe Leu Asp Phe  
 100 105 110  
 Glu Val Ser Val Ile Gly Pro Ser Gln Ser Trp Val Asp Leu Phe Glu  
 115 120 125  
 Gly Gln Val Ile Val Leu Asp Ile Asn Asp Asn Thr Pro Thr Phe Pro  
 130 135 140  
 Ser Pro Val Leu Thr Leu Thr Val Glu Glu Asn Arg Pro Val Gly Thr  
 145 150 155 160  
 Leu Tyr Leu Leu Pro Thr Ala Thr Asp Arg Asp Phe Gly Arg Asn Gly  
 165 170 175  
 Ile Glu Arg Tyr Glu Leu Leu Gln Glu Pro Gly Gly Gly Gly Ser Gly  
 180 185 190  
 Gly Glu Ser Arg Arg Ala Gly Ala Ala Asp Ser Ala Pro Tyr Pro Gly  
 195 200 205  
 Gly Gly Gly Asn Gly Ala Ser Gly Gly Gly Ser Gly Gly Ser Lys Arg  
 210 215 220  
 Arg Leu Asp Ala Ser Glu Gly Gly Gly Gly Thr Asn Pro Gly Gly Arg  
 225 230 235 240  
 Ser Ser Val Phe Glu Leu Gln Val Ala Asp Thr Pro Asp Gly Glu Lys  
 245 250 255  
 Gln Pro Gln Leu Ile Val Lys Gly Ala Leu Asp Arg Glu Gln Arg Asp  
 260 265 270  
 Ser Tyr Glu Leu Thr Leu Arg Val Arg Asp Gly Gly Asp Pro Pro Arg  
 275 280 285  
 Ser Ser Gln Ala Ile Leu Arg Val Leu Ile Thr Asp Val Asn Asp Asn  
 290 295 300  
 Ser Pro Arg Phe Glu Lys Ser Val Tyr Glu Ala Asp Leu Ala Glu Asn  
 305 310 315 320  
 Ser Ala Pro Gly Thr Pro Ile Leu Gln Leu Arg Ala Ala Asp Leu Asp  
 325 330 335

Val Gly Val Asn Gly Gln Ile Glu Tyr Val Phe Gly Ala Ala Thr Glu  
 340 345 350  
 Ser Val Arg Arg Leu Leu Arg Leu Asp Glu Thr Ser Gly Trp Leu Ser  
 355 360 365  
 Val Leu His Arg Ile Asp Arg Glu Glu Val Asn Gln Leu Arg Phe Thr  
 370 375 380  
 Val Met Ala Arg Asp Arg Gly Gln Pro Pro Lys Thr Asp Lys Ala Thr  
 385 390 395 400  
 Val Val Leu Asn Ile Lys Asp Glu Asn Asp Asn Val Pro Ser Ile Glu  
 405 410 415  
 Ile Arg Lys Ile Gly Arg Ile Pro Leu Lys Asp Gly Val Ala Asn Val  
 420 425 430  
 Ala Glu Asp Val Leu Val Asp Thr Pro Ile Ala Leu Val Gln Val Ser  
 435 440 445  
 Asp Arg Asp Gln Gly Glu Asn Gly Val Val Thr Cys Thr Val Val Gly  
 450 455 460  
 Asp Val Pro Phe Gln Leu Lys Pro Ala Ser Asp Thr Glu Gly Asp Gln  
 465 470 475 480  
 Asn Lys Lys Lys Tyr Phe Leu His Thr Ser Thr Pro Leu Asp Tyr Glu  
 485 490 495  
 Ala Thr Arg Glu Phe Asn Val Val Ile Val Ala Val Asp Ser Gly Ser  
 500 505 510  
 Pro Ser Leu Ser Ser Lys Asn Ser Leu Ile Val Lys Val Gly Asp Thr  
 515 520 525  
 Asn Asp Asn Pro Pro Met Phe Gly Gln Ser Val Val Glu Val Tyr Phe  
 530 535 540  
 Pro Glu Asn Asn Ile Pro Gly Glu Arg Val Ala Thr Val Leu Ala Thr  
 545 550 555 560  
 Asp Ala Asp Ser Gly Lys Asn Ala Glu Ile Ala Tyr Ser Leu Asp Ser  
 565 570 575  
 Ser Val Met Gly Ile Phe Ala Ile Asp Pro Asp Ser Gly Asp Ile Leu  
 580 585 590  
 Val Asn Thr Val Leu Asp Arg Glu Gln Thr Asp Arg Tyr Glu Phe Lys  
 595 600 605  
 Val Asn Ala Lys Asp Lys Gly Ile Pro Val Leu Gln Gly Ser Thr Thr  
 610 615 620  
 Val Ile Val Gln Val Ala Asp Lys Asn Asp Asn Asp Pro Lys Phe Met  
 625 630 635 640  
 Gln Asp Val Phe Thr Phe Tyr Val Lys Glu Asn Leu Gln Pro Asn Ser  
 645 650 655

Pro Val Gly Met Val Thr Val Met Asp Ala Asp Lys Gly Arg Asn Ala  
 660 665 670  
 Glu Met Ser Leu Tyr Ile Glu Glu Asn Asn Asn Ile Phe Ser Ile Glu  
 675 680 685  
 Asn Asp Thr Gly Thr Ile Tyr Ser Thr Met Ser Phe Asp Arg Glu His  
 690 695 700  
 Gln Thr Thr Tyr Thr Phe Arg Val Lys Ala Val Asp Gly Gly Asp Pro  
 705 710 715 720  
 Pro Arg Ser Ala Thr Ala Thr Val Ser Leu Phe Val Met Asp Glu Asn  
 725 730 735  
 Asp Asn Ala Pro Thr Val Thr Leu Pro Lys Asn Ile Ser Tyr Thr Leu  
 740 745 750  
 Leu Pro Pro Ser Ser Asn Val Arg Thr Val Val Ala Thr Val Leu Ala  
 755 760 765  
 Thr Asp Ser Asp Asp Gly Ile Asn Ala Asp Leu Asn Tyr Ser Ile Val  
 770 775 780  
 Gly Gly Asn Pro Phe Lys Leu Phe Glu Ile Asp Pro Thr Ser Gly Val  
 785 790 795 800  
 Val Ser Leu Val Gly Lys Leu Thr Gln Lys His Tyr Gly Leu His Arg  
 805 810 815  
 Leu Val Val Gln Val Asn Asp Ser Gly Gln Pro Ser Gln Ser Thr Thr  
 820 825 830  
 Thr Val Val His Val Phe Val Asn Glu Ser Val Ser Asn Ala Thr Ala  
 835 840 845  
 Ile Asp Ser Gln Ile Ala Arg Ser Leu His Ile Pro Leu Thr Gln Asp  
 850 855 860  
 Ile Ala Gly Asp Pro Ser Tyr Glu Ile Ser Lys Gln Arg Leu Ser Ile  
 865 870 875 880  
 Val Ile Gly Val Val Ala Gly Ile Met Thr Val Ile Leu Ile Ile Leu  
 885 890 895  
 Ile Val Val Met Ala Arg Tyr Cys Arg Ser Lys Asn Lys Asn Gly Tyr  
 900 905 910  
 Glu Ala Gly Lys Lys Asp His Glu Asp Phe Phe Thr Pro Gln Gln His  
 915 920 925  
 Asp Lys Ser Lys Lys Pro Lys Lys Asp Lys Lys Asn Lys Lys Ser Lys  
 930 935 940  
 Gln Pro Leu Tyr Ser Ser Ile Val Thr Val Glu Ala Ser Lys Pro Asn  
 945 950 955 960  
 Gly Gln Arg Tyr Asp Ser Val Asn Glu Lys Leu Ser Asp Ser Pro Ser

965                      970                      975  
 Met Gly Arg Tyr Arg Ser Val Asn Gly Gly Pro Gly Ser Pro Asp Leu  
                                  980                                   985                                   990  
 Ala Arg His Tyr Lys Ser Ser Ser Pro Leu Pro Thr Val Gln Leu His  
                                  995                                   1000                                   1005  
 Pro Gln Ser Pro Thr Ala Gly Lys Lys His Gln Ala Val Gln Asp  
                                  1010                                   1015                                   1020  
 Leu Pro Pro Ala Asn Thr Phe Val Gly Ala Gly Asp Asn Ile Ser  
                                  1025                                   1030                                   1035  
 Ile Gly Ser Asp His Cys Ser Glu Tyr Ser Cys Gln Thr Asn Asn  
                                  1040                                   1045                                   1050  
 Lys Tyr Ser Lys Gln Met Arg Leu His Pro Tyr Ile Thr Val Phe  
                                  1055                                   1060                                   1065

Gly

<210> 205  
 <211> 401  
 <212> PRT  
 <213> Homo sapiens

<400> 205

Met Ser Phe Ser Lys Thr His Ser Thr Ala Thr Met Pro Pro Pro Ile  
 1                                   5                                   10                                   15  
 Asn Pro Ile Leu Ala Ser Leu Gln His Asn Ser Ile Leu Thr Pro Thr  
                                  20                                   25                                   30  
 Arg Val Ser Ser Ser Ala Thr Lys Gln Lys Val Leu Ser Pro Pro His  
                                  35                                   40                                   45  
 Ile Lys Ala Asp Phe Asn Leu Ala Asp Phe Glu Cys Glu Glu Asp Pro  
                                  50                                   55                                   60  
 Phe Asp Asn Leu Glu Leu Lys Thr Ile Asp Glu Lys Glu Glu Leu Arg  
                                  65                                   70                                   75                                   80  
 Asn Ile Leu Val Gly Thr Thr Gly Pro Ile Met Ala Gln Leu Leu Asp  
                                  85                                   90                                   95  
 Asn Asn Leu Pro Arg Gly Gly Ser Gly Ser Val Leu Gln Asp Glu Glu  
                                  100                                   105                                   110  
 Val Leu Ala Ser Leu Glu Arg Ala Thr Leu Asp Phe Lys Pro Leu His  
                                  115                                   120                                   125  
 Lys Pro Asn Gly Phe Ile Thr Leu Pro Gln Leu Gly Asn Cys Glu Lys  
                                  130                                   135                                   140  
 Met Ser Leu Ser Ser Lys Val Ser Leu Pro Pro Ile Pro Ala Val Ser  
                                  145                                   150                                   155                                   160  
 Asn Ile Lys Ser Leu Ser Phe Pro Lys Leu Asp Ser Asp Asp Ser Asn



165										170										175									
Gln	Lys	Thr	Ala 180		Lys	Leu	Ala	Ser	Thr 185	Phe	His	Ser	Thr	Ser	Cys 190	Leu													
Arg	Asn	Gly 195	Thr	Phe	Gln	Asn	Ser 200	Leu	Lys	Pro	Ser	Thr 205	Gln	Ser	Ser														
Ala	Ser 210	Glu	Leu	Asn	Gly	His 215	His	Thr	Leu	Gly	Leu 220	Ser	Ala	Leu	Asn														
Leu 225	Asp	Ser	Gly	Thr	Glu 230	Met	Pro	Ala	Leu	Thr 235	Ser	Ser	Gln	Met	Pro 240														
Ser	Leu	Ser	Val 245	Leu	Ser	Val	Cys	Thr	Glu 250	Glu	Ser	Ser	Pro	Pro 255	Asn														
Thr	Gly	Pro	Thr 260	Val	Thr	Pro	Pro	Asn 265	Phe	Ser	Val	Ser	Gln 270	Val	Pro														
Asn	Met	Pro 275	Ser	Cys	Pro	Gln	Ala 280	Tyr	Ser	Glu	Leu	Gln 285	Met	Leu	Ser														
Pro	Ser 290	Glu	Arg	Gln	Cys	Val 295	Glu	Thr	Val	Val	Asn 300	Met	Gly	Tyr	Ser														
Tyr 305	Glu	Cys	Val	Leu	Arg 310	Ala	Met	Lys	Lys	Lys 315	Gly	Glu	Asn	Ile	Glu 320														
Gln	Ile	Leu	Asp	Tyr 325	Leu	Phe	Ala	His	Gly 330	Gln	Leu	Cys	Glu	Lys 335	Gly														
Phe	Asp	Pro	Leu 340	Leu	Val	Glu	Glu	Ala 345	Leu	Glu	Met	His	Gln 350	Cys	Ser														
Glu	Glu	Lys 355	Met	Met	Glu	Phe	Leu 360	Gln	Leu	Met	Ser	Lys 365	Phe	Lys	Glu														
Met	Gly 370	Phe	Glu	Leu	Lys	Asp 375	Ile	Lys	Glu	Val	Leu 380	Leu	Leu	His	Asn														
Asn	Asp	Gln	Asp	Asn	Ala 390	Leu	Glu	Asp	Leu	Met 395	Ala	Arg	Ala	Gly	Ala 400														

Ser

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<210> 206
<211> 285
<212> PRT
<213> Homo sapiens
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<400> 206

Met Glu Val Pro Pro Pro Asp Ala Gly Ser Phe Leu Cys Arg Ala Leu  
1 5 10 15

Cys Leu Phe Pro Arg Val Phe Ala Ala Glu Ala Val Thr Ala Asp Ser  
20 25 30

Glu Val Leu Glu Glu Arg Gln Lys Arg Leu Pro Tyr Val Pro Glu Pro

```

          35              40              45
Tyr Tyr Pro Glu Ser Gly Trp Asp Arg Leu Arg Glu Leu Phe Gly Lys
 50              55              60
Asp Glu Gln Gln Arg Ile Ser Lys Asp Leu Ala Asn Ile Cys Lys Thr
 65              70              75              80
Ala Ala Thr Ala Gly Ile Ile Gly Trp Val Tyr Gly Gly Ile Pro Ala
 85              90              95
Phe Ile His Ala Lys Gln Gln Tyr Ile Glu Gln Ser Gln Ala Glu Ile
100              105              110
Tyr His Asn Arg Phe Asp Ala Val Gln Ser Ala His Arg Ala Ala Thr
115              120              125
Arg Gly Phe Ile Arg Tyr Gly Trp Arg Trp Gly Trp Arg Thr Ala Val
130              135              140
Phe Val Thr Ile Phe Asn Thr Val Asn Thr Ser Leu Asn Val Tyr Arg
145              150              155              160
Asn Lys Asp Ala Leu Ser His Phe Val Ile Ala Gly Ala Val Thr Gly
165              170              175
Ser Leu Phe Arg Ile Asn Val Gly Leu Arg Gly Leu Val Ala Gly Gly
180              185              190
Ile Ile Gly Ala Leu Leu Gly Thr Pro Val Gly Gly Leu Leu Met Ala
195              200              205
Phe Gln Lys Tyr Ser Gly Glu Thr Val Gln Glu Arg Lys Gln Lys Asp
210              215              220
Arg Lys Ala Leu His Glu Leu Lys Leu Glu Glu Trp Lys Gly Arg Leu
225              230              235              240
Gln Val Thr Glu His Leu Pro Glu Lys Ile Glu Ser Ser Leu Gln Glu
245              250              255
Asp Glu Pro Glu Asn Asp Ala Lys Lys Ile Glu Ala Leu Leu Asn Leu
260              265              270
Pro Arg Asn Pro Ser Val Ile Asp Lys Gln Asp Lys Asp
275              280              285
<210> 207
<211> 212
<212> PRT
<213> Homo sapiens
<400> 207
Met Leu Asn Lys Val Leu Ser Arg Leu Gly Val Ala Gly Gln Trp Arg
 1              5              10              15
Phe Val Asp Val Leu Gly Leu Glu Glu Ser Leu Gly Ser Val Pro
 20              25              30
Ala Pro Ala Cys Ala Leu Leu Leu Leu Phe Pro Leu Thr Ala Gln His

```

```

          35              40              45
Glu Asn Phe Arg Lys Lys Gln Ile Glu Glu Leu Lys Gly Gln Glu Val
 50              55              60
Ser Pro Lys Val Tyr Phe Met Lys Gln Thr Ile Gly Asn Ser Cys Gly
 65              70              75              80
Thr Ile Gly Leu Ile His Ala Val Ala Asn Asn Gln Asp Lys Leu Gly
          85              90              95
Phe Glu Asp Gly Ser Val Leu Lys Gln Phe Leu Ser Glu Thr Glu Lys
          100              105              110
Met Ser Pro Glu Asp Arg Ala Lys Cys Phe Glu Lys Asn Glu Ala Ile
          115              120              125
Gln Ala Ala His Asp Ala Val Ala Gln Glu Gly Gln Cys Arg Val Asp
          130              135              140
Asp Lys Val Asn Phe His Phe Ile Leu Phe Asn Asn Val Asp Gly His
          145              150              155              160
Leu Tyr Glu Leu Asp Gly Arg Met Pro Phe Pro Val Asn His Gly Ala
          165              170              175
Ser Ser Glu Asp Thr Leu Leu Lys Asp Ala Ala Lys Val Cys Arg Glu
          180              185              190
Phe Thr Glu Arg Glu Gln Gly Glu Val Arg Phe Ser Ala Val Ala Leu
          195              200              205
Cys Lys Ala Ala
          210

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<210> 208
<211> 596
<212> PRT
<213> Homo sapiens

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<400> 208

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Met Ser Leu Ser Met Arg Asp Pro Val Ile Pro Gly Thr Ser Met Ala
 1              5              10              15
Tyr His Pro Phe Leu Pro His Arg Ala Pro Asp Phe Ala Met Ser Ala
          20              25              30
Val Leu Gly His Gln Pro Pro Phe Phe Pro Ala Leu Thr Leu Pro Pro
          35              40              45
Asn Gly Ala Ala Ala Leu Ser Leu Pro Gly Ala Leu Ala Lys Pro Ile
          50              55              60
Met Asp Gln Leu Val Gly Ala Ala Glu Thr Gly Ile Pro Phe Ser Ser
          65              70              75              80
Leu Gly Pro Gln Ala His Leu Arg Pro Leu Lys Thr Met Glu Pro Glu
          85              90              95
Glu Glu Val Glu Asp Asp Pro Lys Val His Leu Glu Ala Lys Glu Leu

```

100	105	110
Trp Asp Gln Phe His Lys Arg Gly Thr Glu Met Val Ile Thr Lys Ser 115 120 125		
Gly Arg Arg Met Phe Pro Pro Phe Lys Val Arg Cys Ser Gly Leu Asp 130 135 140		
Lys Lys Ala Lys Tyr Ile Leu Leu Met Asp Ile Ile Ala Ala Asp Asp 145 150 155 160		
Cys Arg Tyr Lys Phe His Asn Ser Arg Trp Met Val Ala Gly Lys Ala 165 170 175		
Asp Pro Glu Met Pro Lys Arg Met Tyr Ile His Pro Asp Ser Pro Ala 180 185 190		
Thr Gly Glu Gln Trp Met Ser Lys Val Val Thr Phe His Lys Leu Lys 195 200 205		
Leu Thr Asn Asn Ile Ser Asp Lys His Gly Phe Thr Leu Ala Phe Pro 210 215 220		
Ser Asp His Ala Thr Trp Gln Gly Asn Tyr Ser Phe Gly Thr Gln Thr 225 230 235 240		
Ile Leu Asn Ser Met His Lys Tyr Gln Pro Arg Phe His Ile Val Arg 245 250 255		
Ala Asn Asp Ile Leu Lys Leu Pro Tyr Ser Thr Phe Arg Thr Tyr Leu 260 265 270		
Phe Pro Glu Thr Glu Phe Ile Ala Val Thr Ala Tyr Gln Asn Asp Lys 275 280 285		
Ile Thr Gln Leu Lys Ile Asp Asn Asn Pro Phe Ala Lys Gly Phe Arg 290 295 300		
Asp Thr Gly Asn Gly Arg Arg Glu Lys Arg Gln Gln Leu Thr Leu Gln 305 310 315 320		
Ser Met Arg Val Phe Asp Glu Arg His Lys Lys Glu Asn Gly Thr Ser 325 330 335		
Asp Glu Ser Ser Ser Glu Gln Ala Ala Phe Asn Cys Phe Ala Gln Ala 340 345 350		
Ser Ser Pro Ala Ala Ser Thr Val Gly Thr Ser Asn Leu Lys Asp Leu 355 360 365		
Cys Pro Ser Glu Gly Glu Ser Asp Ala Glu Ala Glu Ser Lys Glu Glu 370 375 380		
His Gly Pro Glu Ala Cys Asp Ala Ala Lys Ile Ser Thr Thr Thr Ser 385 390 395 400		
Glu Glu Pro Cys Arg Asp Lys Gly Ser Pro Ala Val Lys Ala His Leu 405 410 415		

Phe Ala Ala Glu Arg Pro Arg Asp Ser Gly Arg Leu Asp Lys Ala Ser  
420 425 430

Pro Asp Ser Arg His Ser Pro Ala Thr Ile Ser Ser Ser Thr Arg Gly  
435 440 445

Leu Gly Ala Glu Glu Arg Arg Ser Pro Val Arg Glu Gly Thr Ala Pro  
450 455 460

Ala Lys Val Glu Glu Ala Arg Ala Leu Pro Gly Lys Glu Ala Phe Ala  
465 470 475 480

Pro Leu Thr Val Gln Thr Asp Ala Ala Arg Ser Ser Val His Arg His  
485 490 495

Pro Phe Arg Asn Leu Asn Thr Met Arg Pro Arg Leu Arg Tyr Ser Pro  
500 505 510

Tyr Ser Ile Pro Val Pro Val Pro Asp Gly Ser Ser Leu Leu Thr Thr  
515 520 525

Ala Leu Ala Ala Ser Pro Ala Ser Val Ala Val Asp Ser Gly Ser Glu  
530 535 540

Leu Asn Ser Arg Ser Ser Thr Leu Ser Ser Ser Ser Met Ser Leu Ser  
545 550 555 560

Pro Lys Leu Cys Ala Glu Lys Glu Ala Ala Thr Ser Glu Leu Gln Ser  
565 570 575

Ile Gln Arg Leu Val Ser Gly Leu Glu Ala Lys Pro Asp Arg Ser Arg  
580 585 590

Ser Ala Ser Pro  
595

<210> 209  
<211> 215  
<212> PRT  
<213> Homo sapiens

<400> 209

Met Gly Lys Gly Asp Pro Lys Lys Pro Arg Gly Lys Met Ser Ser Tyr  
1 5 10 15

Ala Phe Phe Val Gln Thr Cys Arg Glu Glu His Lys Lys Lys His Pro  
20 25 30

Asp Ala Ser Val Asn Phe Ser Glu Phe Ser Lys Lys Cys Ser Glu Arg  
35 40 45

Trp Lys Thr Met Ser Ala Lys Glu Lys Gly Lys Phe Glu Asp Met Ala  
50 55 60

Lys Ala Asp Lys Ala Arg Tyr Glu Arg Glu Met Lys Thr Tyr Ile Pro  
65 70 75 80

Pro Lys Gly Glu Thr Lys Lys Lys Phe Lys Asp Pro Asn Ala Pro Lys  
85 90 95

Arg Pro Pro Ser Ala Phe Phe Leu Phe Cys Ser Glu Tyr Arg Pro Lys  
 100 105 110  
 Ile Lys Gly Glu His Pro Gly Leu Ser Ile Gly Asp Val Ala Lys Lys  
 115 120 125  
 Leu Gly Glu Met Trp Asn Asn Thr Ala Ala Asp Asp Lys Gln Pro Tyr  
 130 135 140  
 Glu Lys Lys Ala Ala Lys Leu Lys Glu Lys Tyr Glu Lys Asp Ile Ala  
 145 150 155 160  
 Ala Tyr Arg Ala Lys Gly Lys Pro Asp Ala Ala Lys Lys Gly Val Val  
 165 170 175  
 Lys Ala Glu Lys Ser Lys Lys Lys Lys Glu Glu Glu Glu Asp Glu Glu  
 180 185 190  
 Asp Glu Glu Asp Glu Glu Glu Glu Glu Asp Glu Glu Asp Glu Asp Glu  
 195 200 205  
 Glu Glu Asp Asp Asp Asp Glu  
 210 215  
 <210> 210  
 <211> 243  
 <212> PRT  
 <213> Homo sapiens  
 <400> 210  
 Met Ala Ala Ile Ala Ala Ser Glu Val Leu Val Asp Ser Ala Glu Glu  
 1 5 10 15  
 Gly Ser Leu Ala Ala Ala Ala Glu Leu Ala Ala Gln Lys Arg Glu Gln  
 20 25 30  
 Arg Leu Arg Lys Phe Arg Glu Leu His Leu Met Arg Asn Glu Ala Arg  
 35 40 45  
 Lys Leu Asn His Gln Glu Val Val Glu Glu Asp Lys Arg Leu Lys Leu  
 50 55 60  
 Pro Ala Asn Trp Glu Ala Lys Lys Ala Arg Leu Glu Trp Glu Leu Lys  
 65 70 75 80  
 Glu Glu Glu Lys Lys Lys Glu Cys Ala Ala Arg Gly Glu Asp Tyr Glu  
 85 90 95  
 Lys Val Lys Leu Leu Glu Ile Ser Ala Glu Asp Ala Glu Arg Trp Glu  
 100 105 110  
 Arg Lys Lys Lys Arg Lys Asn Pro Asp Leu Gly Phe Ser Asp Tyr Ala  
 115 120 125  
 Ala Ala Gln Leu Arg Gln Tyr His Arg Leu Thr Lys Gln Ile Lys Pro  
 130 135 140  
 Asp Met Glu Thr Tyr Glu Arg Leu Arg Glu Lys His Gly Glu Glu Phe  
 145 150 155 160

Phe Pro Thr Ser Asn Ser Leu Leu His Gly Thr His Val Pro Ser Thr  
165 170 175

Glu Glu Ile Asp Arg Met Val Ile Asp Leu Glu Lys Gln Ile Glu Lys  
180 185 190

Arg Asp Lys Tyr Ser Arg Arg Arg Pro Tyr Asn Asp Asp Ala Asp Ile  
195 200 205

Asp Tyr Ile Asn Glu Arg Asn Ala Lys Phe Asn Lys Lys Ala Glu Arg  
210 215 220

Phe Tyr Gly Lys Tyr Thr Ala Glu Ile Lys Gln Asn Leu Glu Arg Gly  
225 230 235 240

Thr Ala Val

<210> 211  
<211> 479  
<212> PRT  
<213> Homo sapiens

<400> 211

Met Leu Gln Ile Asn Gln Met Phe Ser Val Gln Leu Ser Leu Gly Glu  
1 5 10 15

Gln Thr Trp Glu Ser Glu Gly Ser Ser Ile Lys Lys Ala Gln Gln Ala  
20 25 30

Val Ala Asn Lys Ala Leu Thr Glu Ser Thr Leu Pro Lys Pro Val Gln  
35 40 45

Lys Pro Pro Lys Ser Asn Val Asn Asn Asn Pro Gly Ser Ile Thr Pro  
50 55 60

Thr Val Glu Leu Asn Gly Leu Ala Met Lys Arg Gly Glu Pro Ala Ile  
65 70 75 80

Tyr Arg Pro Leu Asp Pro Lys Pro Phe Pro Asn Tyr Arg Ala Asn Tyr  
85 90 95

Asn Phe Arg Gly Met Tyr Asn Gln Arg Tyr His Cys Pro Val Pro Lys  
100 105 110

Ile Phe Tyr Val Gln Leu Thr Val Gly Asn Asn Glu Phe Phe Gly Glu  
115 120 125

Gly Lys Thr Arg Gln Ala Ala Arg His Asn Ala Ala Met Lys Ala Leu  
130 135 140

Gln Ala Leu Gln Asn Glu Pro Ile Pro Glu Arg Ser Pro Gln Asn Gly  
145 150 155 160

Glu Ser Gly Lys Asp Met Asp Asp Asp Lys Asp Ala Asn Lys Ser Glu  
165 170 175

Ile Ser Leu Val Phe Glu Ile Ala Leu Lys Arg Asn Met Pro Val Ser  
180 185 190

Phe Glu Val Ile Lys Glu Ser Gly Pro Pro His Met Lys Ser Phe Val  
 195 200 205  
 Thr Arg Val Ser Val Gly Glu Phe Ser Ala Glu Gly Glu Gly Asn Ser  
 210 215 220  
 Lys Lys Leu Ser Lys Lys Arg Ala Ala Thr Thr Val Leu Gln Glu Leu  
 225 230 235 240  
 Lys Lys Leu Pro Pro Leu Pro Val Val Glu Lys Pro Lys Leu Phe Phe  
 245 250 255  
 Lys Lys Arg Pro Lys Thr Ile Val Lys Ala Gly Pro Glu Tyr Gly Gln  
 260 265 270  
 Gly Met Asn Pro Ile Ser Arg Leu Ala Gln Ile Gln Gln Ala Lys Lys  
 275 280 285  
 Glu Lys Glu Pro Asp Tyr Val Leu Leu Ser Glu Arg Gly Met Pro Arg  
 290 295 300  
 Arg Arg Glu Phe Val Met Gln Val Lys Val Gly Asn Glu Val Ala Thr  
 305 310 315 320  
 Gly Thr Gly Pro Asn Lys Lys Ile Ala Lys Lys Asn Ala Ala Glu Ala  
 325 330 335  
 Met Leu Leu Gln Leu Gly Tyr Lys Ala Ser Thr Asn Leu Gln Asp Gln  
 340 345 350  
 Leu Glu Lys Thr Gly Glu Asn Lys Gly Trp Ser Gly Pro Lys Pro Gly  
 355 360 365  
 Phe Pro Glu Pro Thr Asn Asn Thr Pro Lys Gly Ile Leu His Leu Ser  
 370 375 380  
 Pro Asp Val Tyr Gln Glu Met Glu Ala Ser Arg His Lys Val Ile Ser  
 385 390 395 400  
 Gly Thr Thr Leu Gly Tyr Leu Ser Pro Lys Asp Met Asn Gln Pro Ser  
 405 410 415  
 Ser Ser Phe Phe Ser Ile Ser Pro Thr Ser Asn Ser Ser Ala Thr Ile  
 420 425 430  
 Ala Arg Glu Leu Leu Met Asn Gly Thr Ser Ser Thr Ala Glu Ala Ile  
 435 440 445  
 Gly Leu Lys Gly Ser Ser Pro Thr Pro Pro Cys Ser Pro Val Gln Pro  
 450 455 460  
 Ser Lys Gln Leu Glu Tyr Leu Ala Arg Ile Gln Gly Phe Gln Val  
 465 470 475



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